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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BERCH Examiner #: 5993 Date: 1/2/03
Art Unit: 1624 Phone Number 308478 Serial Number: 10/047202
Mail Box and Bldg/Room Location: CM15 4E12 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

RECEIVED (GIID) JAN 02 2003 TECH CENTER 1600/2900

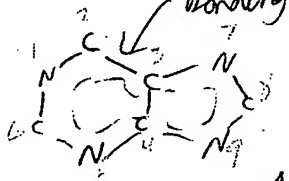
Title of Invention: _____

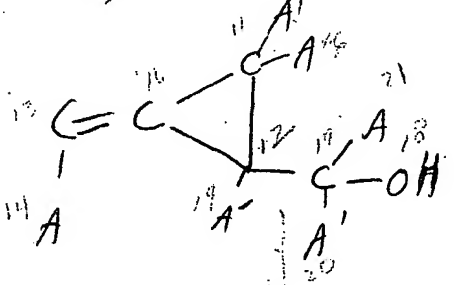
Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

(I) 

(II) 

Cmpd must have both I and II fragments

Mary Jane Ruhl
Tech. Info. Specialist, STIC
TC-1600
CM-1, Room 6A-06
Phone: 605-1155

****

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Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) _____
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

STN _____
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Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

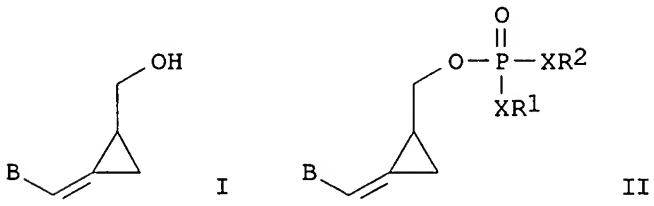
=> d ibib abs hitstr 1-20 l16

L16 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:165041 HCAPLUS
DOCUMENT NUMBER: 136:216595
TITLE: Preparation of 2-hydroxymethylcyclopropylidenemethylpurines and -pyrimidines as antiviral agents
INVENTOR(S): Zemlicka, Jiri; Qiu, Yao-ling; Drach, John C.; Ptak, Roger G.
PATENT ASSIGNEE(S): Wayne State University, USA; The Regents of the University of Michigan
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6352991	B1	20020305	US 1999-267839	19990312
WO 9830563	A1	19980716	WO 1998-US440	19980107
W: CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 2000053603	A1	20000914	WO 2000-US6250	20000310
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1165560	A1	20020102	EP 2000-913872	20000310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002539125	T2	20021119	JP 2000-604040	20000310
US 2002193353	A1	20021219	US 2002-47202	20020114

PRIORITY APPLN. INFO.:
US 1997-35826P P 19970108
US 1997-45676P P 19970506
WO 1998-US440 A2 19980107
US 1999-267839 A 19990312
WO 2000-US6250 W 20000310

OTHER SOURCE(S): MARPAT 136:216595
GI



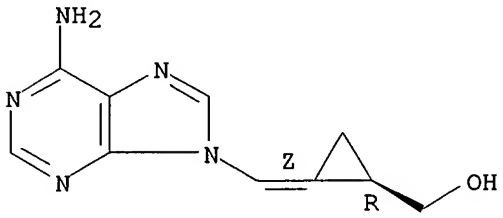
AB Synthesis and antiviral activity of title compds. I and II [wherein B is a purine or pyrimidine heterocyclic ring and is preferably selected from the group consisting of 6-aminopurine (adenine), 2,6-diaminopurine, 2-amino-6-azidopurine, 2-amino-6-cyclopropylaminopurine, 6-hydroxypurine (hypoxanthine), 2-amino-6-halo substituted purines, 2-amino-6-alkoxy substituted purines, 2-amino-6-hydroxypurine (guanine), 3-deazapurines,

7-deaza-purines, 8-azapurines, cytosine, 5-halo substituted cytosines, 5-alkyl substituted cytosines, thymine, uracil and 6-azapyrimidines; X is O; and, R1 and R2 are alkyl or aryl groups; R1X and/or R2X may also be amino acid residues with X = NH] are disclosed. The compds. of the present invention also include the R- and S-enantiomers of the above compds. Thus, II [B = 2,6-diaminopurin-N6-yl, XR1 = Me L-alaninate, XR2 = OPH] (III) is prepd. by reaction of I [B = 2,6-diaminopurin-N6-yl] with phenylmethoxyalaninyl phosphorochloridate. III demonstrated an IC50 = 0.26 .mu.M against HIV-1.

IT **203305-34-4P 219727-86-3P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antiviral agents hydroxymethylcyclopropylidenemethylpurines and -pyrimidines via derivatization of bromomethylbromocyclopropane carboxylates)

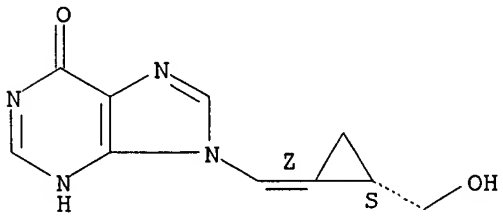
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 219727-86-3 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

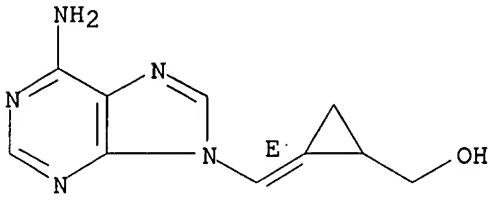


IT **200434-67-9P 200434-69-1P 200434-97-5P**
200435-01-4P 200496-39-5P 203305-38-8P
210355-01-4P 210355-04-7P 210355-05-8P
247091-19-6P 289888-78-4P 289888-79-5P
289888-80-8P 289888-82-0P 289888-83-1P
289888-84-2P 291307-16-9P 291307-17-0P
292825-45-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antiviral agents hydroxymethylcyclopropylidenemethylpurines and -pyrimidines via derivatization of bromomethylbromocyclopropane carboxylates)

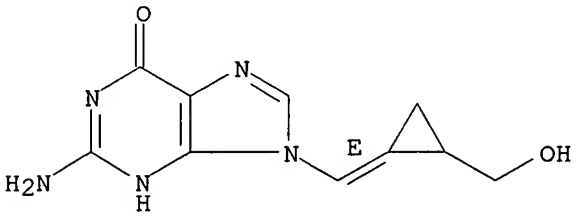
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



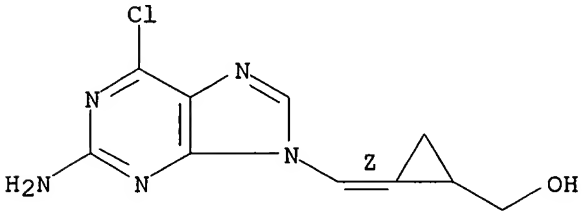
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



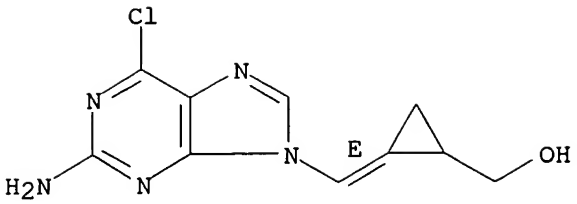
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



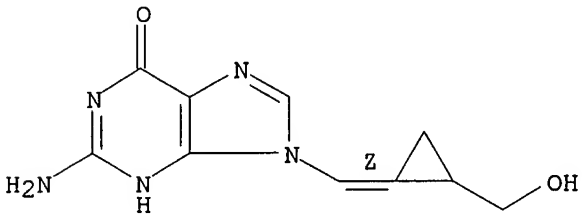
RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



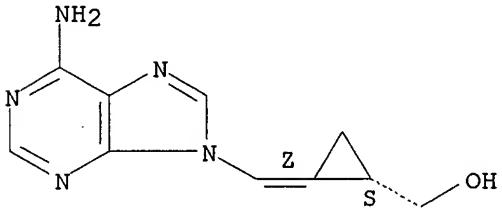
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



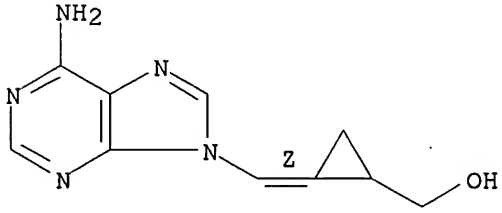
RN 203305-38-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



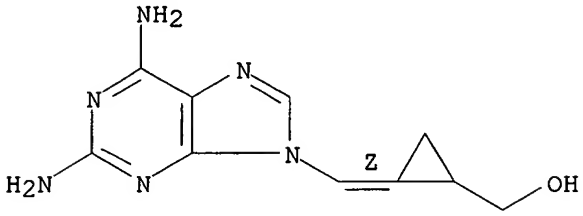
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



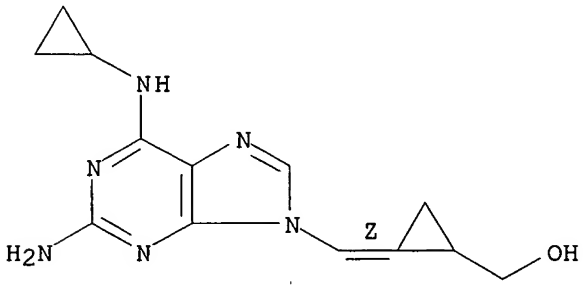
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



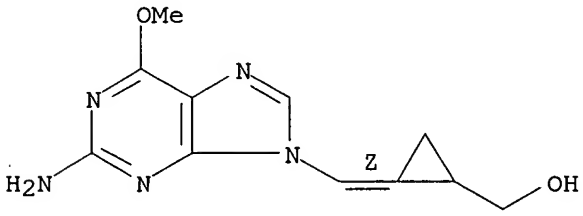
RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-
yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



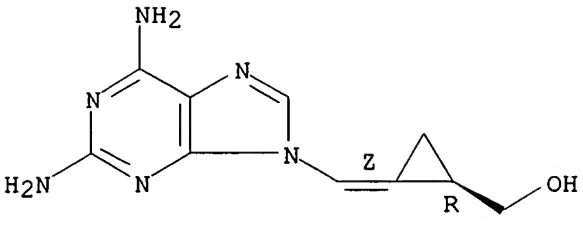
RN 247091-19-6 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-,
(2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



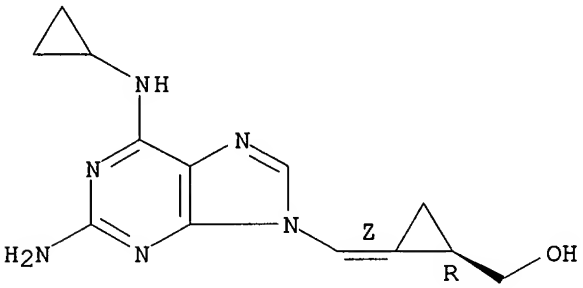
RN 289888-78-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1R,2Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



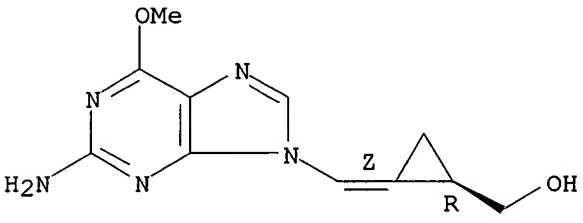
RN 289888-79-5 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



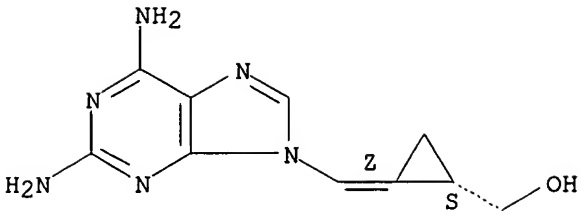
RN 289888-80-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



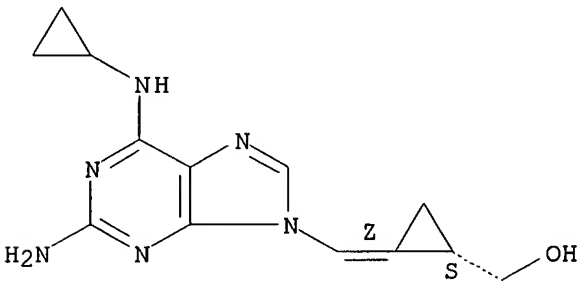
RN 289888-82-0 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



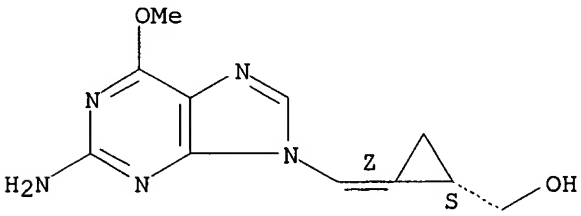
RN 289888-83-1 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



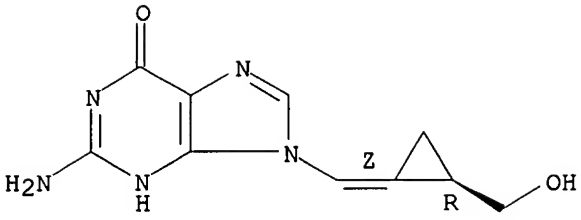
RN 289888-84-2 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



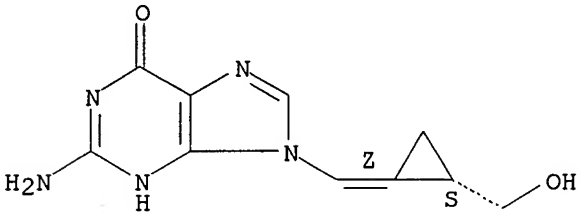
RN 291307-16-9 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2R)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



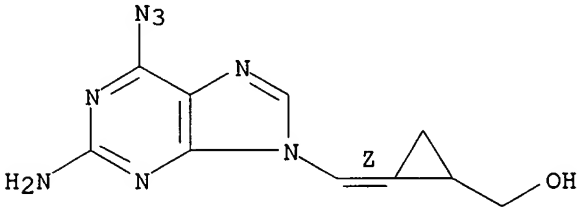
RN 291307-17-0 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



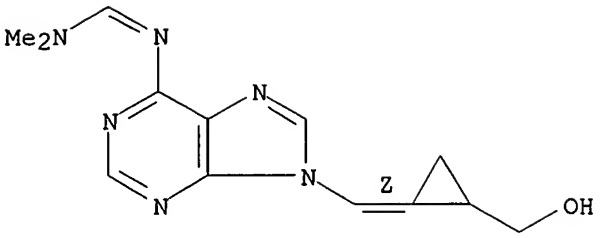
RN 292825-45-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-azido-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



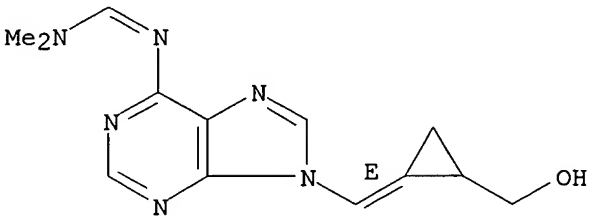
IT **200434-90-8P 200434-92-0P 289888-77-3P**
289888-81-9P 292825-46-8P 292825-47-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antiviral agents hydroxymethylcyclopropylidenemethylpurines and -pyrimidines via derivatization of bromomethylbromocyclopropane carboxylates)
RN 200434-90-8 HCAPLUS
CN Methanimidamide, N'-[9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



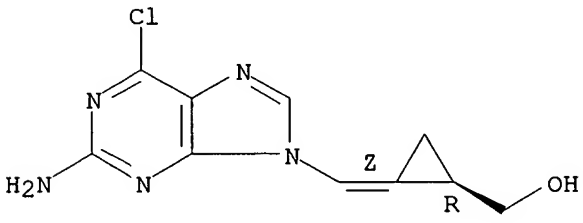
RN 200434-92-0 HCAPLUS
CN Methanimidamide, N'-[9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



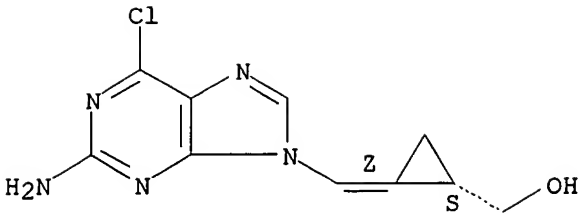
RN 289888-77-3 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



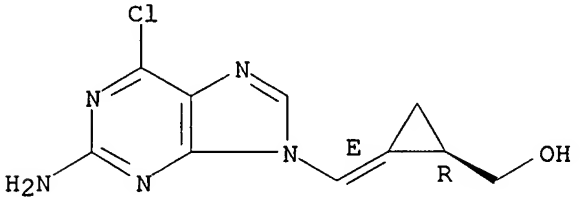
RN 289888-81-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



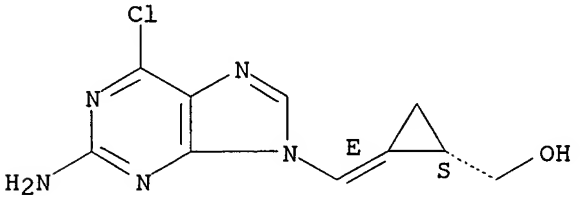
RN 292825-46-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1R,2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 292825-47-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:899542 HCAPLUS
DOCUMENT NUMBER: 136:167065
TITLE: Revision of Absolute Configuration of Enantiomeric (Methylenecyclopropyl)carbinols Obtained from (R)-(-)- and (S)-(+)-Epichlorohydrin and Methylenetriphenylphosphorane. Implications for Reaction Mechanism and Improved Synthesis of Antiviral Methylenecyclopropane Analogues of Nucleosides
AUTHOR(S): Chen, Xinchao; Zemlicka, Jiri
CORPORATE SOURCE: Department of Chemistry Developmental Therapeutics Program Barbara Ann Karmanos Cancer Institute, Wayne

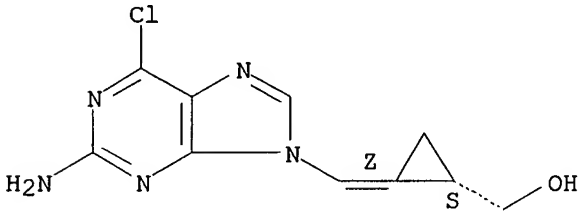
State University School of Medicine, Detroit, MI, 48201-1379, USA
SOURCE: Journal of Organic Chemistry (2002), 67(1), 286-289
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Abs. configurations of enantiomeric methylenecyclopropanecarbinols obtained by reaction of (R)- and (S)-epichlorohydrin with methylenetriphenylphosphorane or resoln. of the corresponding oxaphospholane 6 via a salt with L-(+)-tartaric acid and subsequent Wittig transformation with formaldehyde were revised. The (-)-oxaphospholane 6 has the S,S and (-)-(methylenecyclopropyl)carbinol (4) the R configuration. The configurations of (+)-6 and (+)-4 are then R,R and S, resp. These assignments are in accord with an initial attack of phosphorane at the oxirane ring of epichlorohydrin. An improved prepn. of key enantiomeric intermediates important for synthesis of antiviral purine methylenecyclopropane analogs of nucleosides, is also described.

IT **289888-81-9P 292825-47-9P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(revision of abs. configuration of enantiomeric (methylenecyclopropyl)carbinols obtained from alkylation of epichlorohydrin with methylenetriphenylphosphorane)

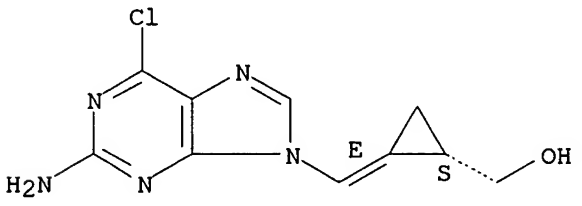
RN 289888-81-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 292825-47-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2E)- (9CI) (CA INDEX NAME)

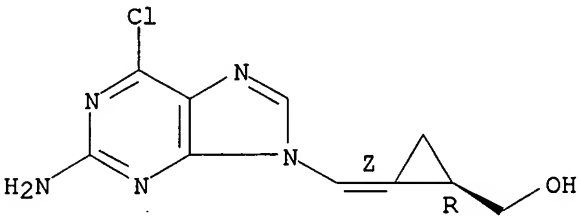
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **289888-77-3P**

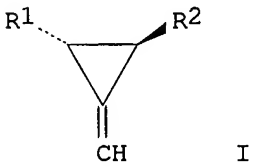
RL: SPN (Synthetic preparation); PREP (Preparation)
(revision of abs. configuration of enantiomeric (methylenecyclopropyl)carbinols obtained from alkylation of epichlorohydrin with methylenetriphenylphosphorane)
RN 289888-77-3 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:675129 HCAPLUS
DOCUMENT NUMBER: 136:37861
TITLE: Synthesis and antiviral activity of novel exomethylene cyclopropyl nucleosides
AUTHOR(S): Choi, Bo Gil; Kwak, Eun Yee; Hong, Joon Hee; Lee, Chong Kyo
CORPORATE SOURCE: Department of Medicinal Chemistry, College of Pharmacy, Chonnam National University, Kwangju, 500-757, S. Korea
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 1059-1062
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



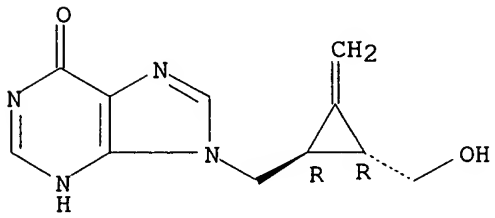
I

AB Novel cyclopropyl nucleosides were synthesized as potential antiviral agents. The key intermediate I (R1 = CH2OSiPh2t-Bu, R2 = CH2OSO2p-C6H5Me), prepd. from Feist's acid I (R1 = R2 = CO2H) was condensed with purine derivs. by the SN2 type reaction. All the synthesized compds. were evaluated for antiviral activity.
IT **380378-47-2P 380378-49-4P 380378-50-7P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of exomethylene cyclopropyl nucleosides via Feist's acid condensation with purine derivs. by the SN2 type reaction as antiviral agents)

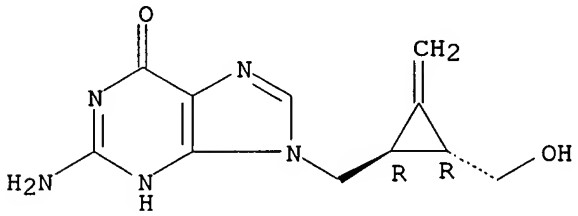
RN 380378-47-2 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[[(1R,2R)-2-(hydroxymethyl)-3-methylenecyclopropyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



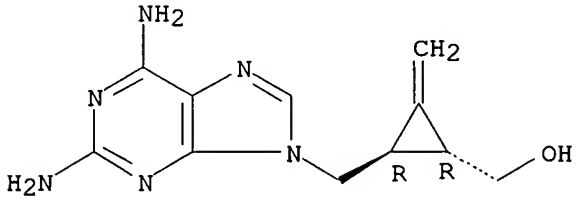
RN 380378-49-4 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[(1R,2R)-2-(hydroxymethyl)-3-methylenecyclopropyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380378-50-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)- (9CI) (CA INDEX NAME)

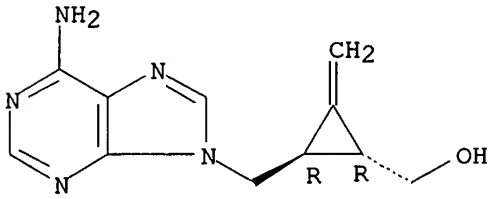
Absolute stereochemistry.



IT **380378-45-0P 380378-46-1P 380378-48-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of exomethylene cyclopropyl nucleosides via Feist's acid condensation with purine derivs. by the SN2 type reaction as antiviral agents)

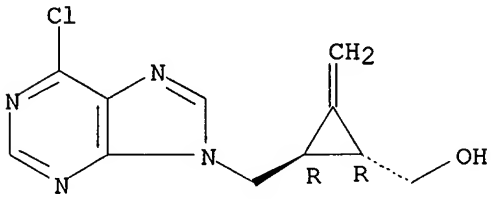
RN 380378-45-0 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



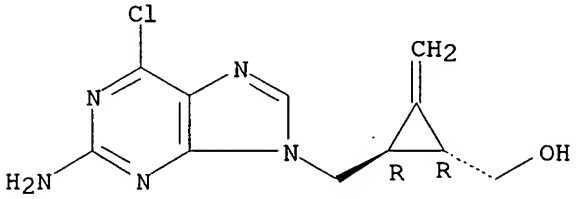
RN 380378-46-1 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-chloro-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380378-48-3 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)- (9CI) (CA INDEX NAME)

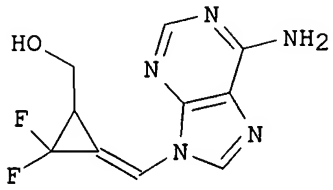
Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:674873 HCAPLUS
DOCUMENT NUMBER: 136:6256
TITLE: Synthesis and antiviral activity of methylenedifluorocyclopropane analogs of nucleosides
AUTHOR(S): Wang, R.; Ksebati, M. B.; Drach, J. C.; Zemlicka, J.
CORPORATE SOURCE: Barbara Ann Karmanos Cancer Institute, School of Medicine, Wayne State University, Detroit, MI, 48201-1379, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001),

20(4-7), 329-332
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

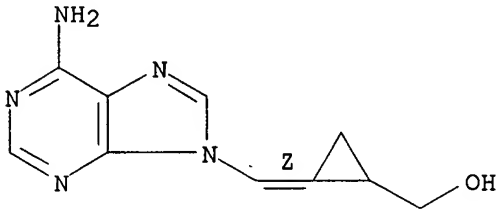
AB Synthesis and antiviral activity of methylenedifluorocyclopropane analogs, e.g. I, are described.

IT **210355-01-4**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(synthesis and antiviral activity of methylenedifluorocyclopropane analogs of nucleosides)

RN 210355-01-4 HCAPLUS

CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:11061 HCAPLUS
DOCUMENT NUMBER: 134:147799
TITLE: Synthesis and antiviral activity of novel methylene cyclopropyl nucleosides
AUTHOR(S): Kwak, Eun Yee; Hong, Joon Hee; Lee, Chong Kyo; Choi, Bo Gil
CORPORATE SOURCE: Department of Medicinal Chemistry, College of Pharmacy, Chonnam National University, Kwangju, 500-757, S. Korea
SOURCE: Archives of Pharmacal Research (2000), 23(6), 559-563
CODEN: APHRDQ; ISSN: 0253-6269
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:147799

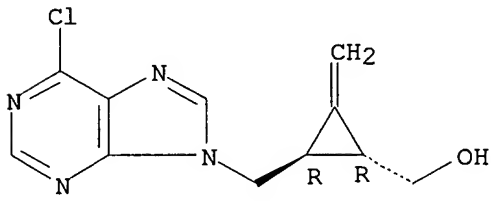
AB Novel exomethylene cyclopropyl nucleosides were synthesized as potential antiviral agents. The key intermediate, trans-1-[(tert-butyldiphenylsilyl)oxymethyl]-2-[(p-toluenesulfonyl)oxymethyl]-3-methylenecyclopropane, was synthesized in 4 steps, from Feist's acid and was condensed with purine derivs. by the SN2 type reaction to give some cyclopropyl nucleosides. The synthesized nucleosides did not show any significant antiviral activity against HSV-1, HSV-2, HCMV, HIV-1, HIV-2, and HBV up to 100 .mu.M.

IT **324536-72-3P 324536-82-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antiviral activity of novel methylene cyclopropyl nucleosides)

RN 324536-72-3 HCAPLUS

CN Cyclopropanemethanol, 2-[(6-chloro-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

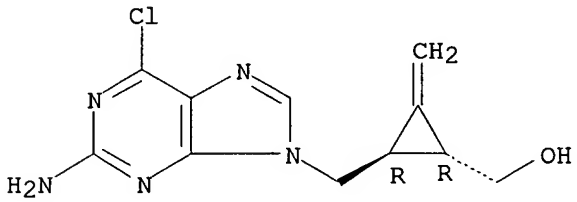
Relative stereochemistry.



RN 324536-82-5 HCAPLUS

CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

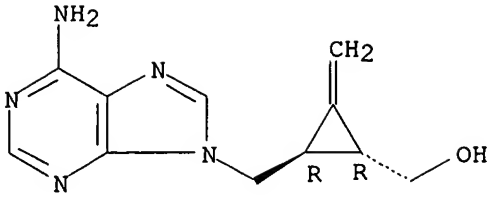


IT **324536-67-6P 324536-77-8P 324536-87-0P**
324536-91-6P 324536-95-0P 324536-99-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antiviral activity of novel methylene cyclopropyl nucleosides)

RN 324536-67-6 HCAPLUS

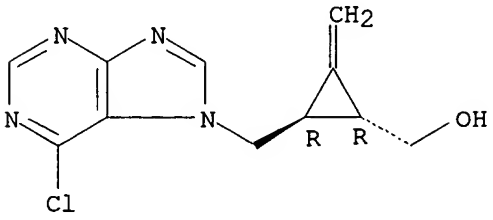
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



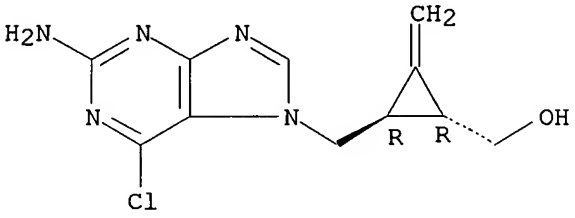
RN 324536-77-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-chloro-7H-purin-7-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



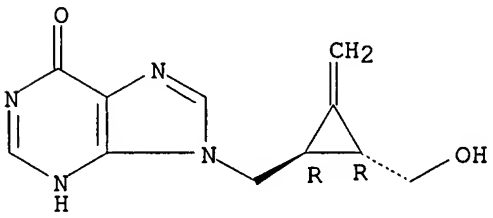
RN 324536-87-0 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-7H-purin-7-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 324536-91-6 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[[(1R,2R)-2-(hydroxymethyl)-3-methylenecyclopropyl]methyl]-, rel- (9CI) (CA INDEX NAME)

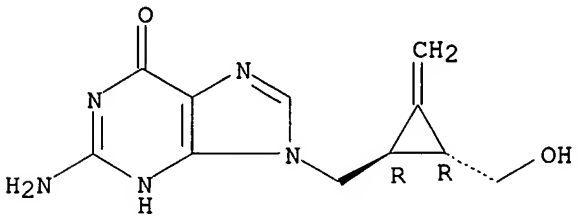
Relative stereochemistry.



RN 324536-95-0 HCAPLUS

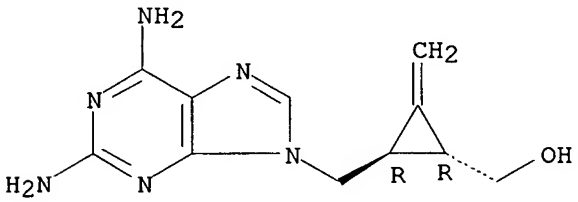
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[[(1R,2R)-2-(hydroxymethyl)-3-methylenecyclopropyl]methyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 324536-99-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methyl]-3-methylene-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

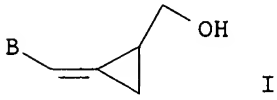


REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

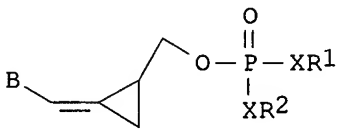
L16 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:646011 HCAPLUS
DOCUMENT NUMBER: 133:237772
TITLE: synthesis of 2-hydroxymethylcyclopropylidenemethyl-purines and -pyrimidines as antiviral agents
INVENTOR(S): Zemlicka, Jiri; Qiu, Yao-Ling; Drach, John C.; Ptak, Roger G.
PATENT ASSIGNEE(S): Regents of the University of Michigan, USA; Wayne State University
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053603	A1	20000914	WO 2000-US6250	20000310
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6352991	B1	20020305	US 1999-267839	19990312
EP 1165560	A1	20020102	EP 2000-913872	20000310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
JP 2002539125 T2 20021119 JP 2000-604040 20000310
PRIORITY APPLN. INFO.: US 1999-267839 A 19990312
US 1997-35826P P 19970108
US 1997-45676P P 19970506
WO 1998-US440 A2 19980107
WO 2000-US6250 W 20000310
OTHER SOURCE(S): MARPAT 133:237772
GI



I



II

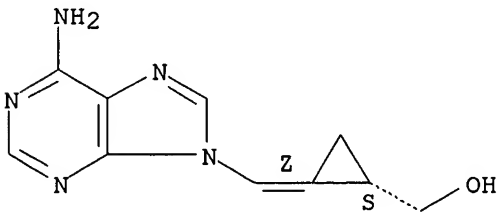
AB Synthesis and antiviral activity of title compds. (I) and (II) [B = purine or pyrimidine heterocyclic ring and is preferably selected from the group consisting of 6-aminopurine (adenine), 2,6-diaminopurine, 2-amino-6-azidopurine, 2-amino-6-cyclopropylaminopurine, 6-hydroxypurine (hypoxanthine), 2-amino-6-halo substituted purines, 2-amino-6-alkoxy substituted purines, 2-amino-6-hydroxypurine (guanine), 3-deazapurines, 7-deaza-purines, 8-azapurines, cytosine, 5-halo substituted cytosines, 5-alkyl substituted cytosines, thymine, uracil and 6-azapyrimidines; X = O; R1 and R2 = alkyl or aryl groups; R1X and/or R2X can also be amino acid residues with X as NH] is disclosed. The compds. of the present invention also include the syn- and anti- isomers as well as the R- and S-enantiomers of the above compds. Thus, II (B = adenine-N9-yl, XR1 = Me L-alaninate, XR2 = OPh) (III) is prepd. by reaction of I (B = adenine-N9-yl) (IV) with Ph methoxyalaninylphosphorochloridate. III shows an IC50 of 2.5.upsilon.M against HSV-1.

IT **203305-38-8P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(synthesis of hydroxymethylcyclopropylidenemethyl- purines and -pyrimidines as antiviral agents)

RN 203305-38-8 HCAPLUS

CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

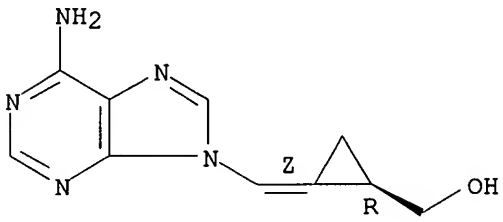


IT **203305-34-4P 219727-86-3P**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of hydroxymethylcyclopropylidenemethyl- purines and -pyrimidines as antiviral agents)

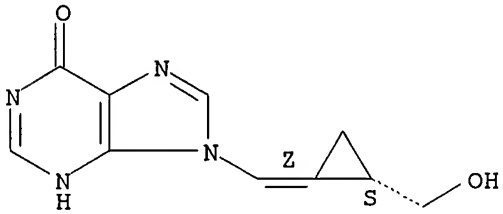
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 219727-86-3 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

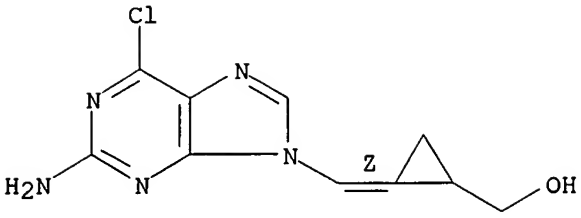
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **200434-97-5P 210355-01-4P 210355-04-7P 289888-78-4P 289888-82-0P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of hydroxymethylcyclopropylidenemethyl- purines and -pyrimidines as antiviral agents)

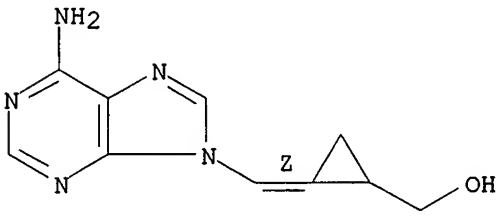
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



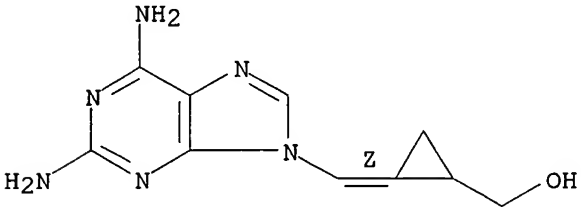
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



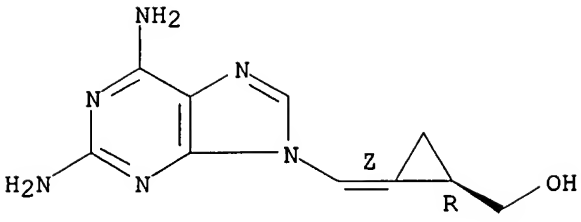
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



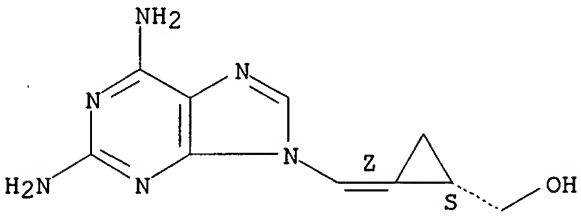
RN 289888-78-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



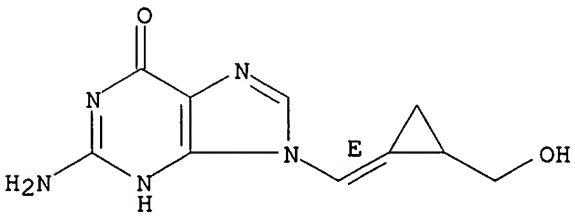
RN 289888-82-0 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1S,2Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **200434-69-1P 210355-05-8P 247091-19-6P**
289888-77-3P 289888-79-5P 289888-80-8P
289888-81-9P 289888-83-1P 289888-84-2P
291307-16-9P, R-(-)-Synguanol **291307-17-0P**,
S-(+)-Synguanol **292825-45-7P 292825-46-8P**
292825-47-9P 292862-60-3P, (.+-.)-Synguanol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of hydroxymethylcyclopropylidenemethyl- purines and -pyrimidines as antiviral agents)
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropyliden
e]methyl]- (9CI) (CA INDEX NAME)

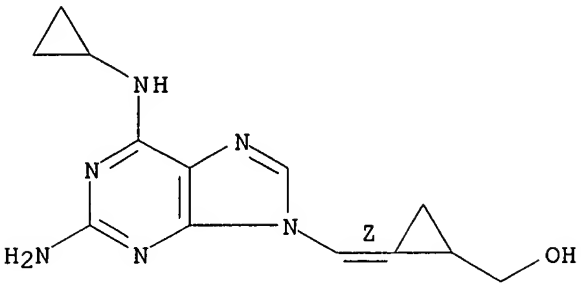
Double bond geometry as shown.



RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-

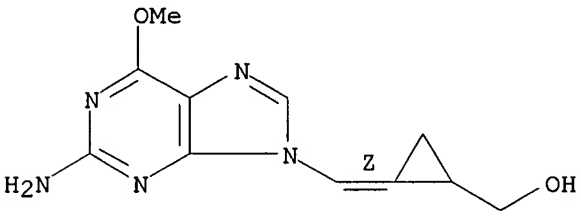
yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



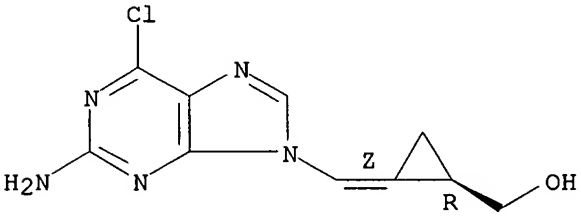
RN 247091-19-6 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



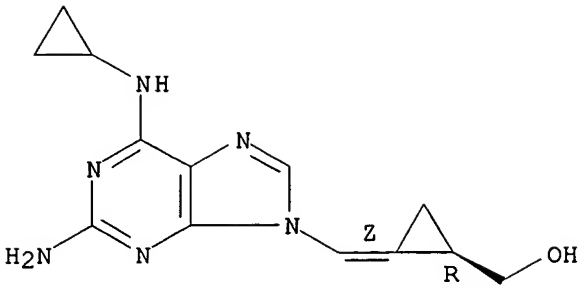
RN 289888-77-3 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



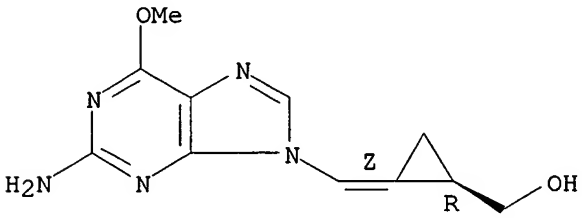
RN 289888-79-5 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



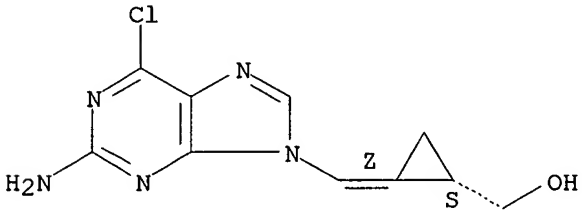
RN 289888-80-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



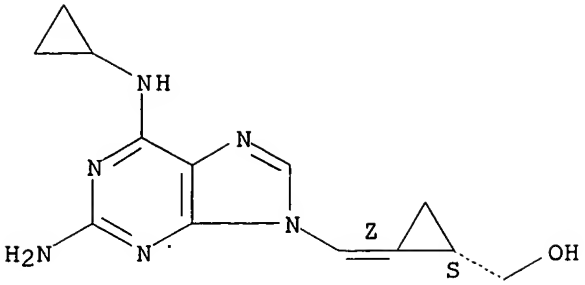
RN 289888-81-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



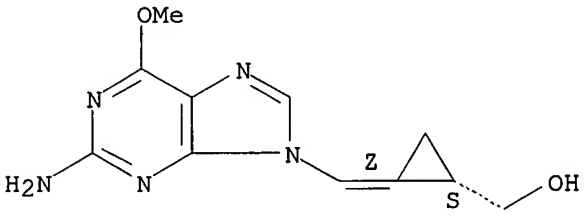
RN 289888-83-1 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



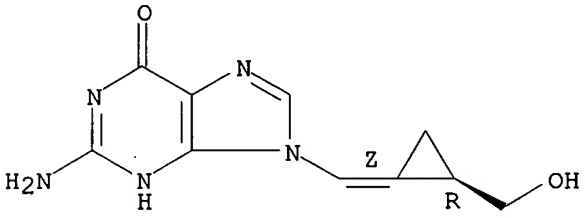
RN 289888-84-2 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



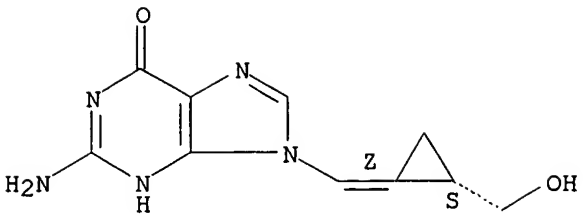
RN 291307-16-9 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2R)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



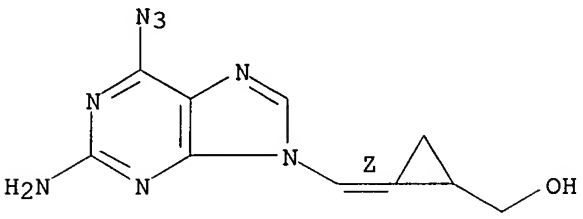
RN 291307-17-0 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



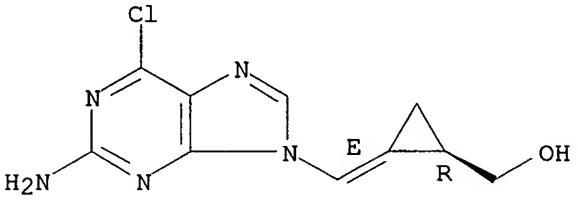
RN 292825-45-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-azido-9H-purin-9-yl)methylene]-, (2Z)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



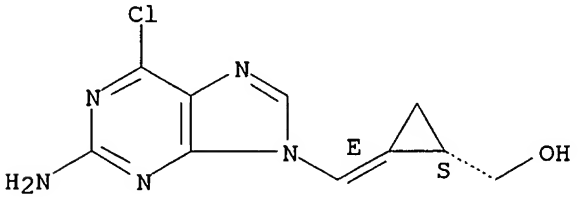
RN 292825-46-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-,
(1R,2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



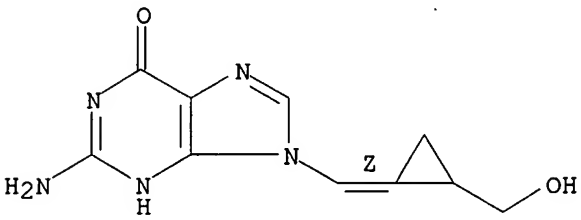
RN 292825-47-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-,
(1S,2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



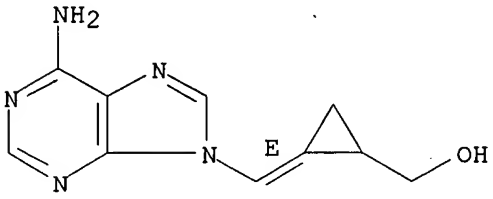
RN 292862-60-3 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



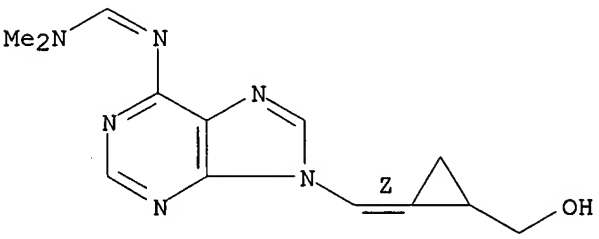
IT **200434-67-9P 200434-90-8P 200434-92-0P**
200435-01-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of hydroxymethylcyclopropylidenemethyl- purines and -pyrimidines as antiviral agents)
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



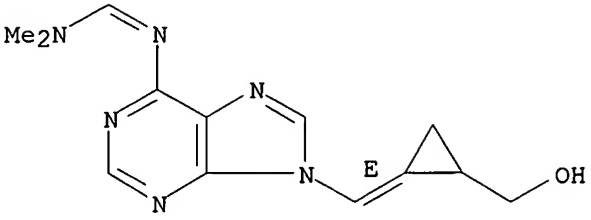
RN 200434-90-8 HCAPLUS
CN Methanimidamide, N'-[9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



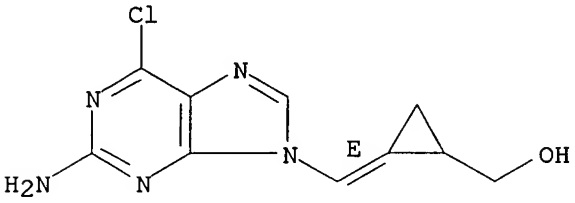
RN 200434-92-0 HCAPLUS
CN Methanimidamide, N'-[9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

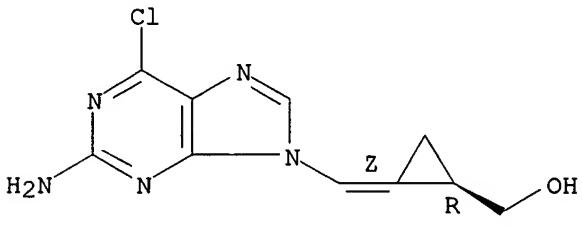
L16 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:477487 HCAPLUS
DOCUMENT NUMBER: 133:217269
TITLE: Synthesis and enantioselectivity of the antiviral effects of (R,Z)-,(S,Z)-methylenecyclopropane analogues of purine nucleosides and phosphoralaninate prodrugs: influence of heterocyclic base, type of virus and host cells
AUTHOR(S): Qiu, Y-L.; Geiser, F.; Kira, T.; Gullen, E.; Cheng, Y-C.; Ptak, R. G.; Breitenbach, J. M.; Drach, J. C.; Hartline, C. B.; Kern, E. R.; Zemlicka, J.
CORPORATE SOURCE: Department of Chemistry, Experimental and Clinical Chemotherapy Program, Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, USA
SOURCE: Antiviral Chemistry & Chemotherapy (2000), 11(3), 191-202
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of R and S enantiomers of 2-aminopurine methylenecyclopropane analogs of nucleosides was synthesized. Two diastereoisomeric lipophilic phosphate prodrugs derived from R and S enantiomers of 2,6-diaminopurine analog were also prepd. Enantioselectivity (diastereoselectivity in case of prodrugs) of in vitro antiviral effects was investigated with human and murine cytomegalovirus (HCMV and MCMV, resp.), herpes simplex virus types 1 and 2 (HSV-1 and HSV-2, resp.), human immunodeficiency virus type 1

(HIV-1), hepatitis B virus (HBV), Epstein-Barr virus (EBV) and varicella zoster virus (VZV). Strong differences in enantioselectivity were found between the R and S enantiomers of adenine analog and enantiomeric 2-aminopurine analogs. Thus, the enantiomers of adenine analog were equipotent against HCMV but not MCMV, where the S enantiomer is strongly preferred. The same S preference was found throughout the 2-aminopurine series for both HCMV and MCMV. In contrast, R-synadenol in HIV-1 assays was the best agent, whereas the S enantiomers of moderately effective 2-amino-6-cyclopropylamino and 2-amino-6-methoxypurine analogs were preferred. Little enantiomeric preference was found for R and S enantiomers of synadenol and the corresponding enantiomers of 2,6-diaminopurine analog against HBV. A mixed pattern of enantioselectivity was obsd. for EBV depending on the type of host cells and assay. Against VZV, the R and S enantiomers of adenine analog were equipotent or almost equipotent, but throughout the series of 2-aminopurine analogs a distinct preference for the S enantiomers was found. The stereoselectivity pattern of both diastereoisomeric prodrugs mostly followed enantioselectivity of the parent analogs. The varying enantioselectivities in the series of purine methylenecyclopropane analogs are probably a consequence of differences in the mechanisms of action in different virus/host cell systems.

IT **289888-77-3P 289888-78-4P 289888-79-5P**
289888-80-8P 289888-81-9P 289888-82-0P
289888-83-1P 289888-84-2P 291307-16-9P,
(R)-(-)-Synguanol **291307-17-0P,** (S)-(+)-Synguanol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antiviral structure-activity relations of methylenecyclopropane analogs of purine nucleosides and phosphoralaninate prodrugs)

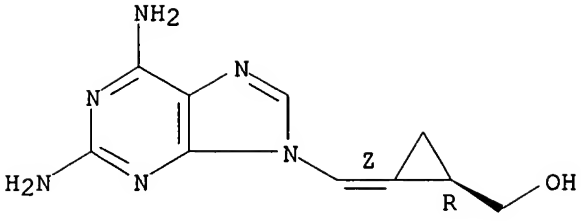
RN 289888-77-3 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



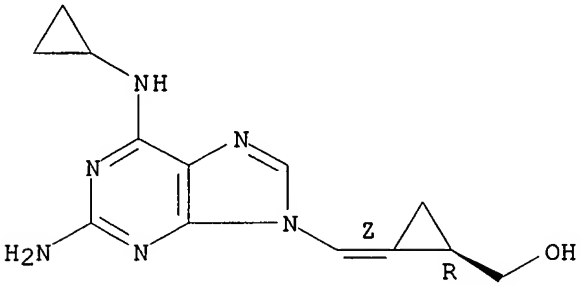
RN 289888-78-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



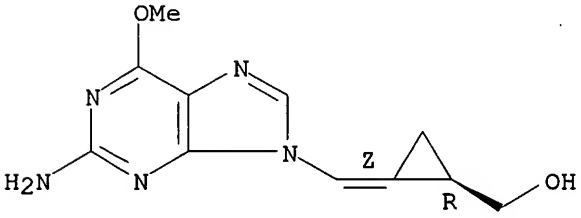
RN 289888-79-5 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



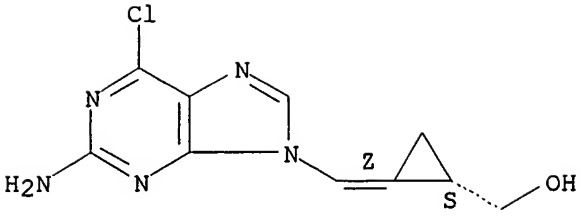
RN 289888-80-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



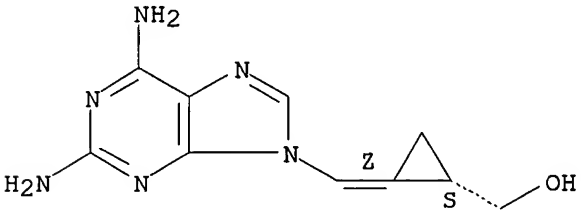
RN 289888-81-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



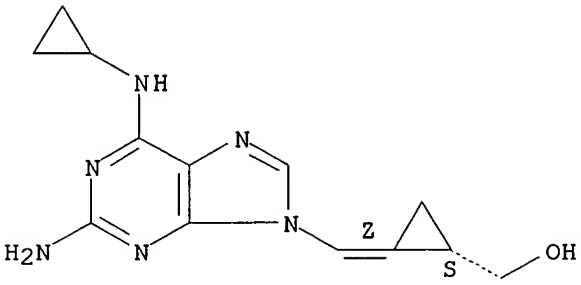
RN 289888-82-0 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (1S,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



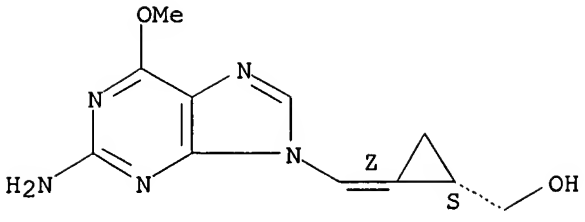
RN 289888-83-1 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



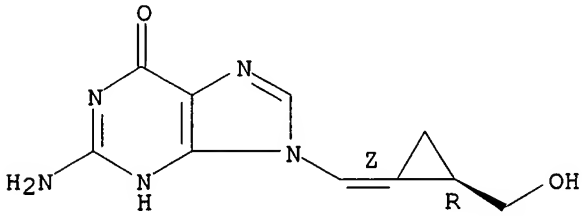
RN 289888-84-2 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (1S,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



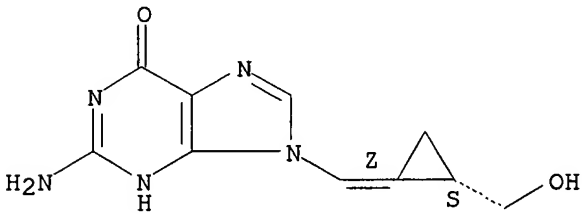
RN 291307-16-9 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2R)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



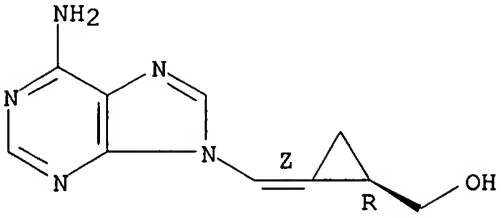
RN 291307-17-0 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



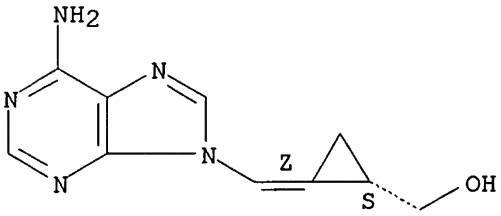
IT **203305-34-4**, (R)-Synadenol **203305-38-8**, (S)-Synadenol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and antiviral structure-activity relations of methylenecyclopropane analogs of purine nucleosides and phosphoralaninate prodrugs)
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 203305-38-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

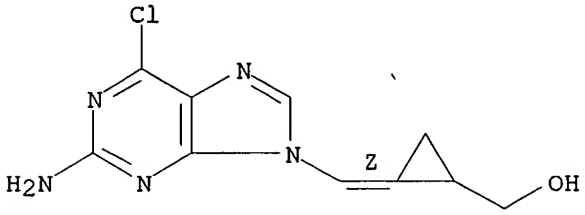
L16 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:367587 HCAPLUS
DOCUMENT NUMBER: 133:99138
TITLE: In vitro activities of methylenecyclopropane analogues of nucleosides and their phosphoralaninate prodrugs against cytomegalovirus and other herpesvirus infections
AUTHOR(S): Rybak, Rachel J.; Hartline, Caroll B.; Qiu, Yao-Ling; Zemlicka, Jiri; Harden, Emma; Marshall, Gwen; Sommadossi, Jean-Pierre; Kern, Earl R.
CORPORATE SOURCE: School of Medicine, University of Alabama, Birmingham, AL, 35294-2170, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1506-1511
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human cytomegalovirus (HCMV) infection does not generally cause problems in the immunocompetent adult but can result in severe clin. disease in the fetus, neonate, and immunocompromised host. Ganciclovir (GCV), the agent currently used to treat most HCMV infections, has resulted in much therapeutic success; however, efficacy remains suboptimal. Therefore, there is still a need to develop new compds. for use against HCMV infections. In the present study, several Z- and E-series methylenecyclopropane analogs and their phosphoroalaninate prodrugs were tested initially for activity against HCMV, strain AD169, and murine

cytomegalovirus (MCMV) in vitro. Many were found to exhibit efficacy comparable to that of GCV against HCMV in plaque assays and were active against MCMV as well. The compds. were also tested for efficacy against herpes simplex virus types 1 and 2, varicella-zoster virus, and Epstein-Barr virus, and some had levels of activity that were comparable to that of acyclovir. In addn., the compds. synguanol (QYL-438) and 2-amino-6-cyclopropylamino analog (QYL-769) were chosen for further evaluation and were found to be effective against addnl. lab. and clin. isolates of HCMV and GCV-resistant isolates. QYL-438 and QYL-769 were found to be nontoxic in human and mouse fibroblasts and were considerably less toxic than GCV in granulocyte macrophage CFUs and erythroid burst-forming units. These results provide evidence for the high activity of some of these methylenecyclopropane analogs against various herpesviruses, particularly HCMV, in tissue culture and suggest that further evaluation is warranted to det. their potential for use in future clin. studies.

IT **200434-97-5**, QYL 418 **200496-39-5**, QYL 438
203305-34-4, QYL 587A **203305-38-8**, QYL 788
210355-01-4, QYL 284A **210355-04-7**, QYL 546
210355-05-8, QYL 769 **247091-19-6**, QYL 941
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activities of methylenecyclopropane analogs of nucleosides and their phosphoralaninate prodrugs against cytomegalovirus and other herpesvirus infections)

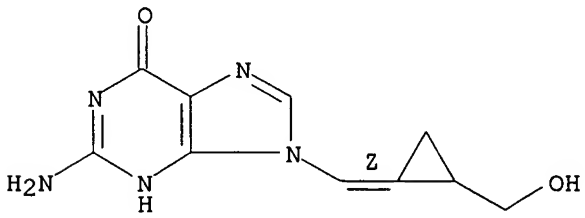
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



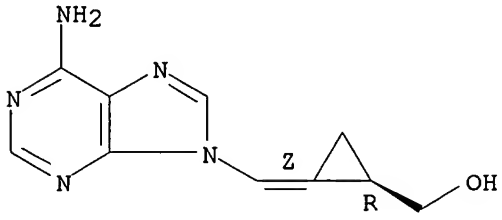
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



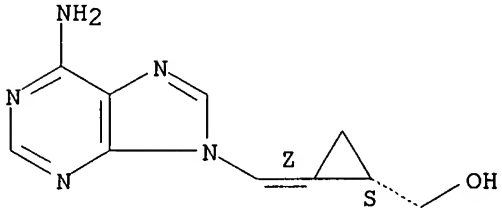
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



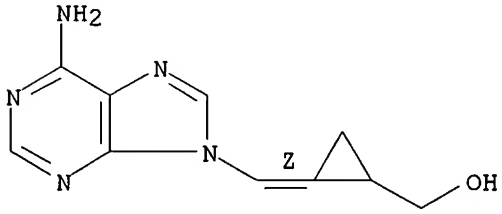
RN 203305-38-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



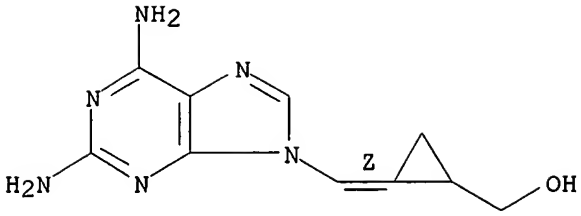
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.



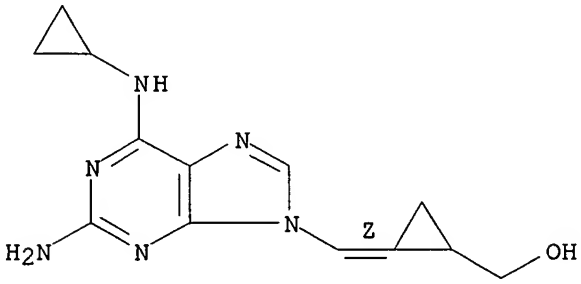
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



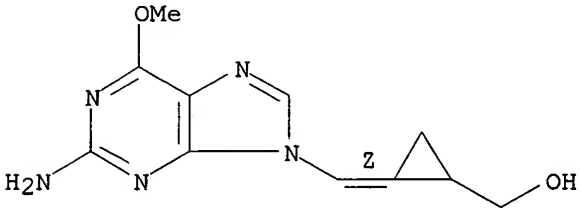
RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 247091-19-6 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:623639 HCAPLUS
DOCUMENT NUMBER: 132:44527
TITLE: Effective treatment of murine cytomegalovirus infections with methylenecyclopropane analogs of nucleosides
AUTHOR(S): Rybak, R. J.; Zemlicka, J.; Qiu, Y.-L.; Hartline, C. B.; Kern, E. R.
CORPORATE SOURCE: Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, USA

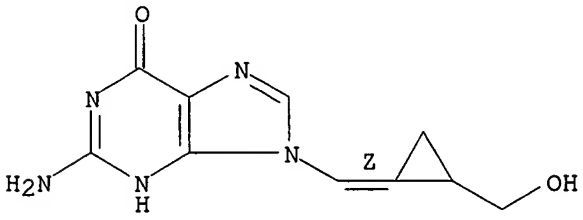
SOURCE: Antiviral Research (1999), 43(3), 175-188
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A no. of new nucleoside analogs with a Z- or E-methylenecyclopropane structure exhibited significant activity against human and murine cytomegaloviruses (HCMV, MCMV) in tissue culture that was generally comparable to, or greater than, 9-[(1-3-dihydroxy-2-propoxy)methyl]guanine (ganciclovir, GCV). Several of these analogs were chosen for further evaluation of therapeutic efficacy utilizing a MCMV infection. I.p. inoculation of 3-wk-old Balb/c mice with 2.0 .times. 105 plaque forming units (pfu) of MCMV results in an acute, lethal infection with rapid virus replication in visceral and glandular tissue, thus, making it an ideal model for identifying compds. that have potential for use in humans. Synadenol (QYL-284A) and synguanol (QYL-438) were administered i.p. once daily for 5 days initiated 6, 24, or 48 h post-viral infection. Significant protection was demonstrated at 50 and 16.7 mg/kg compared to placebo, with efficacy comparable to GCV. When delivered orally once or twice daily at 100 mg/kg per day, QYL-438 was active, but less effective than GCV. In addn., 2-amino-6-methoxypurine analog (QYL-941) was active at 60 mg/kg administered orally twice daily, comparable to GCV, while its prodrug (QYL-972) was as effective as GCV at 40 mg/kg when delivered twice daily for 5 days. Addnl., analog 2-amino-6-cyclopropylaminopurine (QYL-769) was highly efficacious when given orally twice daily for 5 days. Mortality of 0% and 13% was obsd. at 60 and 20 mg/kg, resp., which was similar to GCV. Oral treatment with QYL-769 or GCV reduced virus replication in target organs, but neither resulted in complete clearance of MCMV. These data indicate that these new analogs have activity comparable to GCV when given orally to mice and should be evaluated further to assess their potential for use in humans.

IT **200496-39-5**, Synguanol **210355-01-4**, QYL 284A
210355-05-8, QYL 769 **247091-19-6**, QYL 941
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effective treatment of murine cytomegalovirus infections with methylenecyclopropane analogs of nucleosides)

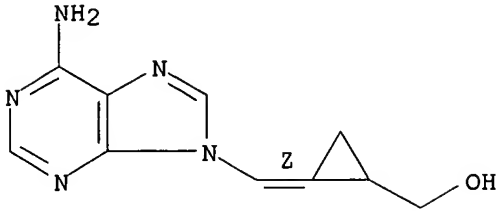
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



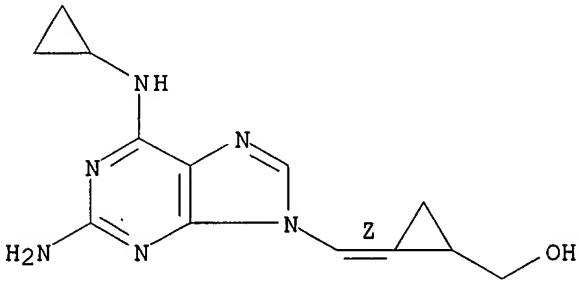
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



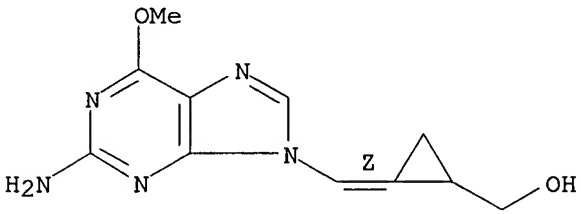
RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 247091-19-6 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:449762 HCAPLUS
DOCUMENT NUMBER: 131:295153
TITLE: Synthesis and antiviral activity of phosphoralaninate derivatives of methylenecyclopropane analogues of nucleosides
AUTHOR(S): Qiu, Yao-Ling; Ptak, Roger G.; Breitenbach, Julie M.; Lin, Ju-Sheng; Cheng, Yung-Chi; Drach, John C.; Kern, Earl R.; Zemlicka, Jiri

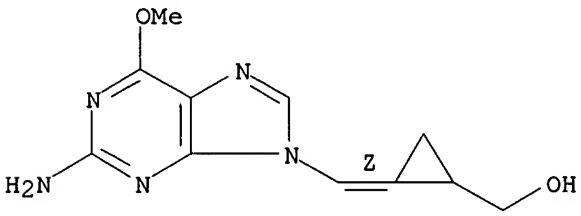
CORPORATE SOURCE: Barbara Ann Karmanos Cancer Institute, Experimental and Clinical Chemotherapy Program, Department of Chemistry, Wayne State University School of Medicine, Detroit, MI, USA
SOURCE: Antiviral Research (1999), 43(1), 37-53
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phenylmethylphosphoro-L-alaninate prodrugs of antiviral Z-methylenecyclopropane nucleoside analogs and their inactive E-isomers were synthesized and evaluated for their antiviral activity against HCMV, HSV-1, HSV-2, HHV-6, EBV, VZV, HIV-1 and HBV. The adenine Z-analog was a potent inhibitor of all these viruses but it displayed cellular toxicity. The guanine Z-deriv. was active against HCMV, HBV, EBV and VZV and it was not cytotoxic. The 2,6-diaminopurine analog was the most potent against HIV-1 and HBV and somewhat less against HHV-6, HCMV, EBV and VZV in a non-cytotoxic concn. range. The 2-amino-6-cyclopropylamino and 2-amino-6-methoxypurine prodrugs were also more active than parent analogs against several viruses but with a less favorable cytotoxicity profile. In the E-series of analogs, adenine deriv. was active against HIV-1, HBV and EBV, and it was non-cytotoxic. The guanine analog exhibited a significant effect only against HBV. The 2,6-diaminopurine E-analog was inactive with the exception of a single EBV assay. The 2-amino-6-methoxypurine Z-methylenecyclopropane nucleoside analog was an effective inhibitor of HCMV, MCMV and EBV. The 2,6-diaminopurine Z-prodrug seems to be the best candidate for further development.

IT **247091-19-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and antiviral activity of prodrug phosphoralaninate derivs. of methylenecyclopropane analogs of nucleosides in relation to cellular toxicity)

RN 247091-19-6 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-methoxy-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

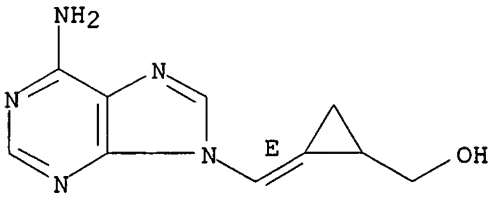
Double bond geometry as shown.



IT **200434-67-9 200434-69-1 200434-97-5**
200496-39-5, Synguanol **210355-05-8 213484-30-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis and antiviral activity of prodrug phosphoralaninate derivs. of methylenecyclopropane analogs of nucleosides in relation to cellular

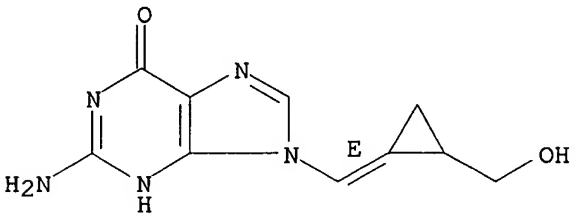
toxicity)
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



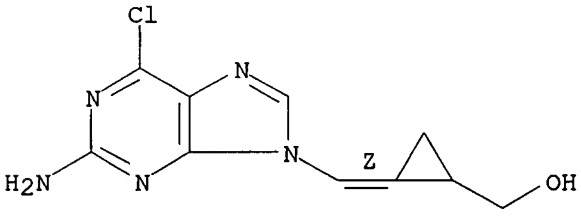
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



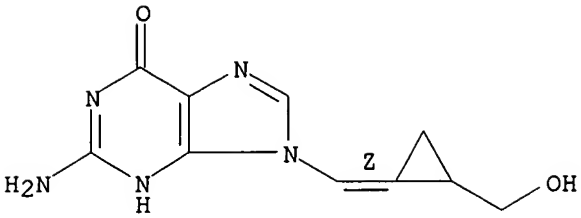
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



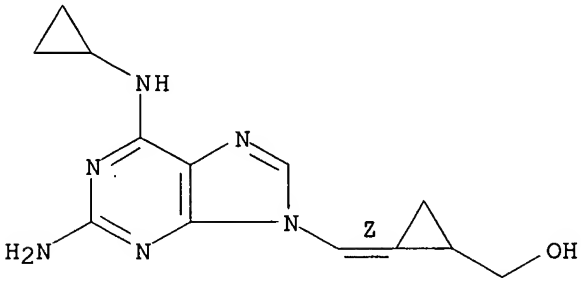
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



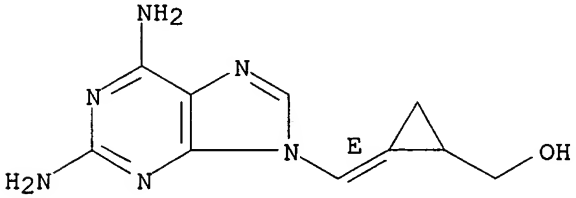
RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



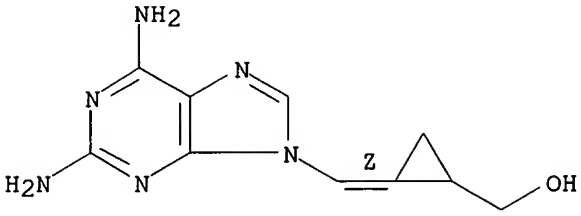
RN 213484-30-1 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **210355-04-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and antiviral activity of prodrug phosphoralaninate derivs. of methylenecyclopropane analogs of nucleosides in relation to cellular toxicity)
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



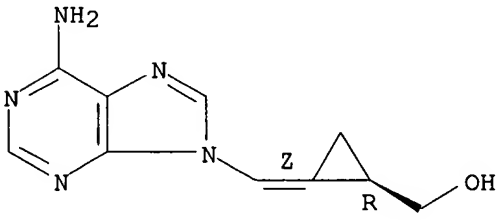
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:448586 HCAPLUS
DOCUMENT NUMBER: 131:116435
TITLE: Methylenecyclopropane analogues of nucleosides: synthesis, absolute configuration, and enantioselectivity of antiviral effect of (R)-(-)- and (S)-(+)-synadenol
AUTHOR(S): Qiu, Y.-L.; Hempel, A.; Camerman, N.; Camerman, A.; Geiser, F.; Ptak, R. G.; Breitenbach, J. M.; Kira, T.; Li, L.; Gullen, E.; Cheng, Y.-C.; Drach, J. C.; Zemlicka, J.
CORPORATE SOURCE: Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, 48201-1379, USA
SOURCE: Nucleosides & Nucleotides (1999), 18(4 & 5), 597-598
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthesis, abs. configuration, and antiviral activity of enantiomeric antiviral agents (R)-(-)- and (S)-(+)-synadenol are described.

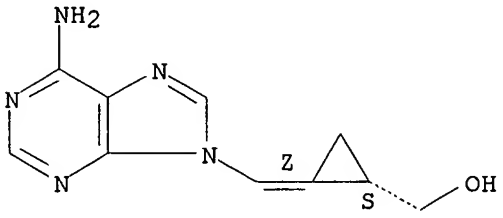
IT **203305-34-4P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(synthesis,abs. configuration, and enantioselectivity of antiviral effect of (R)-(-)- and (S)-(+)-synadenol)
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



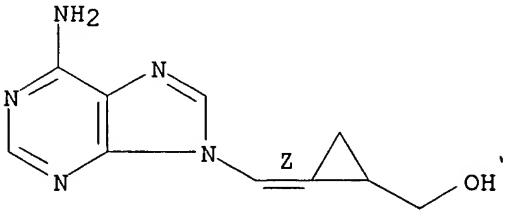
IT **203305-38-8P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis,abs. configuration, and enantioselectivity of antiviral effect of (R)-(-)- and (S)-(+)-synadenol)
RN 203305-38-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



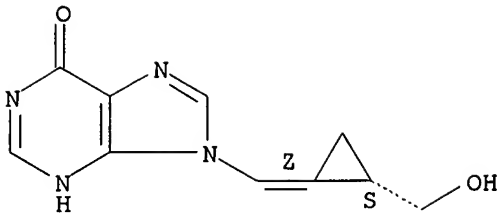
IT **210355-01-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis,abs. configuration, and enantioselectivity of antiviral effect of (R)-(-)- and (S)-(+)-synadenol)
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **219727-86-3P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis,abs. configuration, and enantioselectivity of antiviral effect of (R)-(-)- and (S)-(+)-synadenol)
RN 219727-86-3 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

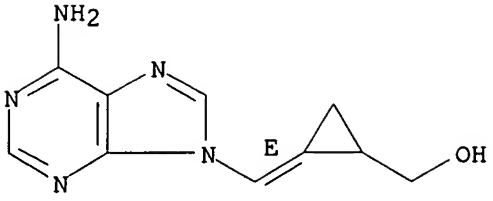
L16 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:369441 HCAPLUS
DOCUMENT NUMBER: 131:138935
TITLE: In vitro anti-human immunodeficiency virus activities of Z- and E-methylenecyclopropane nucleoside analogs and their phosphoro-L-alaninate diesters
AUTHOR(S): Uchida, Hiroyuki; Kodama, Eiichi N.; Yoshimura, Kazuhisa; Maeda, Yosuke; Kosalaraksa, Pope; Maroun, Victor; Qiu, Yao-Ling; Zemlicka, Jiri; Mitsuya, Hiroaki
CORPORATE SOURCE: The Experimental Retrovirology Section, Department of Developmental Therapeutics, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(6), 1487-1490
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nucleoside analogs with a Z- or an E-methylenecyclopropane moiety were synthesized and examd. for activity against human immunodeficiency virus type 1 (HIV-1) in vitro. The addn. of a Me Ph phosphoro-L-alaninate moiety to modestly active analogs resulted in potentiation of their anti-HIV-1 activity. Two such compds., designated QYL-685 (with 2,6-diaminopurine) and QYL-609 (with adenine), were most potent against HIV-1 in vitro, with 50% inhibitory concns. of 0.034 and 0.0026 .mu.M, resp., in MT-2 cell-based assays. Both compds. were active against zidovudine-resistant, didanosine-resistant, and multi-dideoxynucleoside-resistant infectious clones in vitro. Further development of these analogs as potential therapies for HIV-1 infection is warranted.

IT **200434-67-9 200434-69-1 200496-39-5 210355-01-4 210355-04-7 213484-30-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(in vitro anti-HIV1 activities of Z- and E-methylenecyclopropane nucleoside analogs and their phosphoro-L-alaninate diesters)

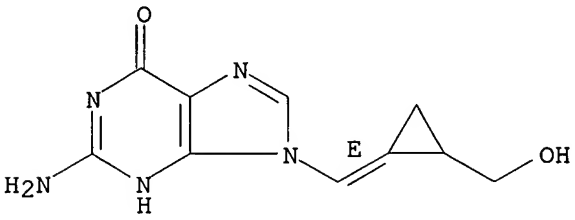
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



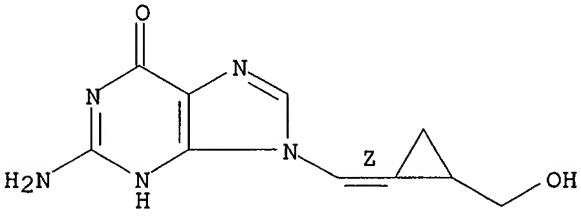
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



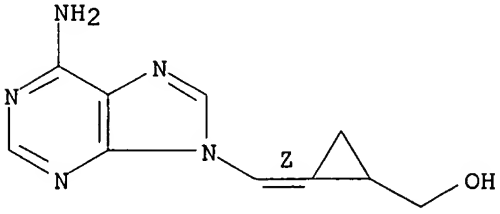
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



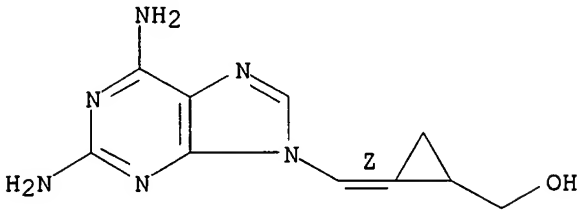
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



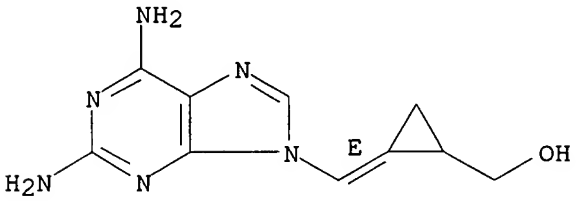
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



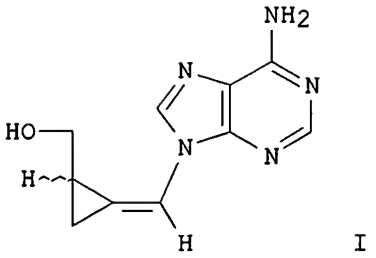
RN 213484-30-1 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2E)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:756435 HCAPLUS
DOCUMENT NUMBER: 130:110515
TITLE: (R)-(-)- and (S)-(+)-Synadenol: Synthesis, Absolute Configuration, and Enantioselectivity of Antiviral Effect
AUTHOR(S): Qiu, Yao-Ling; Hempel, Andrew; Camerman, Norman; Camerman, Arthur; Geiser, Fiona; Ptak, Roger G.; Breitenbach, Julie M.; Kira, Toshiko; Li, Ling; Gullen, Elizabeth; Cheng, Yung-Chi; Drach, John C.; Zemlicka, Jiri
CORPORATE SOURCE: Department of Chemistry Experimental and Clinical Chemotherapy Program Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI, 48201-1379, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(26), 5257-5264
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

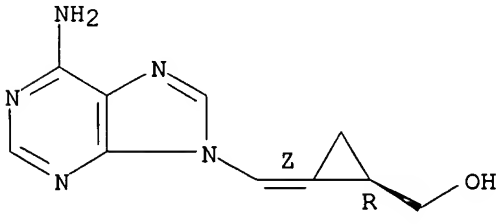
AB Synthesis of (R)-(-)- and (S)-(+)-synadenol (I, 95-96% ee) is described. Abs. configuration of (R)-I was established by two methods: (i) synthesis from (R)-methylenecyclopropanecarboxylic acid and (ii) X-ray diffraction of a single crystal of (-)-synadenol hydrochloride. Racemic methylenecyclopropanecarboxylic acid was resolved by a modification of the described procedure. The latter forms a pseudosym. dimer with adenine-adenine base pairing in the lattice with the nucleobase in an anti-like conformation. Enantiomers I exhibit varied enantioselectivity toward different viruses. Both enantiomers are equipotent against human cytomegalovirus (HCMV) and varicella zoster virus (VZV). The S-enantiomer 2a is somewhat more effective than R-enantiomer I in herpes simplex virus 1 and 2 (HSV-1 and HSV-2) assays. By contrast, enantioselectivity of antiviral effect is reversed in Epstein-Barr virus (EBV) and human immunodeficiency virus type 1 (HIV-1) assays where the R-enantiomer I is preferred. In these assays, the S-enantiomer I is less effective (EBV) or devoid of activity (HIV-1).

IT **203305-34-4P 203305-38-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, abs. configuration, and antiviral enantioselectivity of (R)-(-)- and (S)-(+)-synadenol)

RN 203305-34-4 HCAPLUS

CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)-(9CI) (CA INDEX NAME)

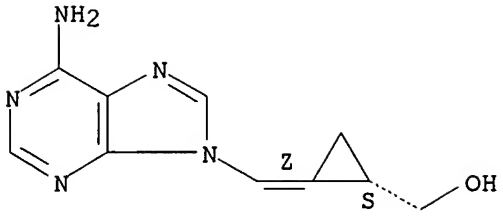
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 203305-38-8 HCAPLUS

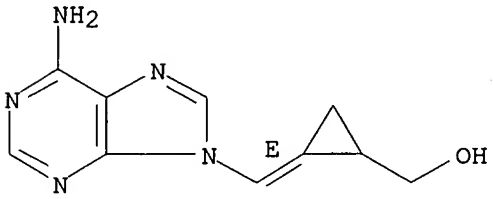
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



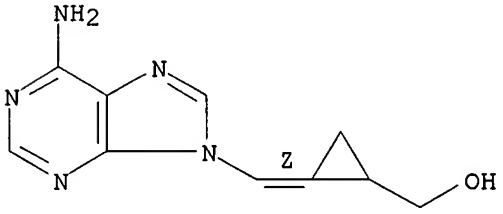
IT **200434-67-9 210355-01-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, abs. configuration, and antiviral enantioselectivity of (R)-(-)- and (S)-(+)-synadenol)
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



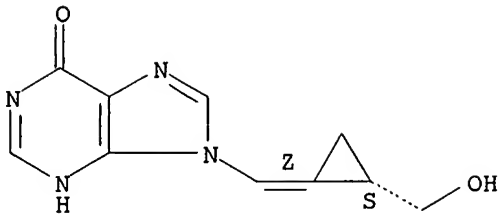
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



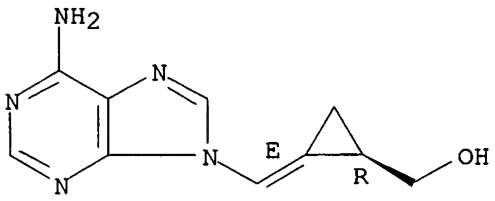
IT **219727-86-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, abs. configuration, and antiviral enantioselectivity of (R)-(-)- and (S)-(+)-synadenol)
RN 219727-86-3 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[(Z)-[(2S)-(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **203305-37-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, abs. configuration, and antiviral enantioselectivity of (R)-(-)- and (S)-(+)-synadenol)
RN 203305-37-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

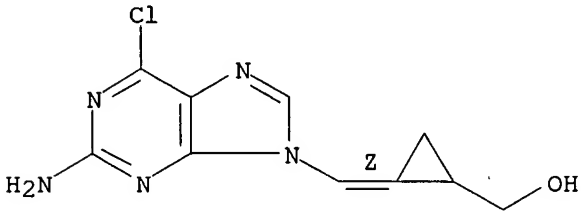


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:677967 HCAPLUS
DOCUMENT NUMBER: 130:14154
TITLE: A new efficient synthesis of antiviral methylenecyclopropane analogs of purine nucleosides
AUTHOR(S): Qiu, Yao-Ling; Zemlicka, Jiri
CORPORATE SOURCE: Department Chemistry, Experimental Clinical Chemotherapy Program, Barbara Ann Karmanos Cancer Institute, School Medicine, Wayne State University, Detroit, MI, 48201, USA
SOURCE: Synthesis (1998), (10), 1447-1452
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:14154
AB A new synthetic approach to the antiviral agents synadenol and its 2-amino-6-chloropurine analog is described. Alkylating agents were obtained by redn. of 2-bromo-2-(bromomethyl)cyclopropane-1-carboxylates followed by protection of the OH function. Partial halogen exchange at the 2-bromomethyl group was obsd. with reagents contg. Cl. These agents were employed in an alkylation-elimination sequence with adenine or 2-amino-6-chloropurine to give the desired compds. after deprotection.
IT **200434-97-5P 200435-01-4P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP

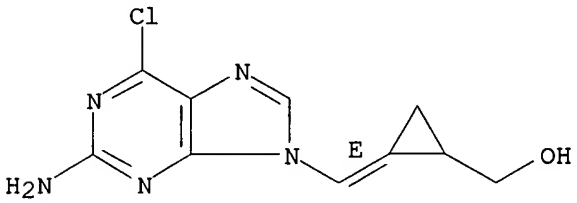
(Preparation)
(prepn. of methylenecyclopropane analogs of purine nucleosides)
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



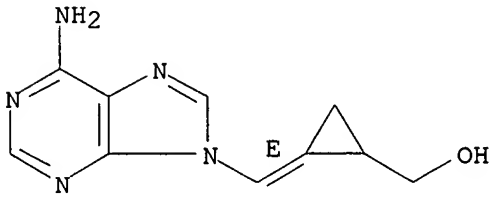
RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



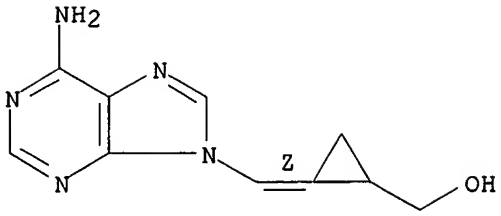
IT **200434-67-9P 210355-01-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of methylenecyclopropane analogs of purine nucleosides)
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:513223 HCAPLUS
DOCUMENT NUMBER: 129:254348
TITLE: (Z)- and (E)-2-(hydroxymethylcyclopropylidene)-methylpurines and pyrimidines as antiviral agents
AUTHOR(S): Qiu, Y.-L.; Ptak, R. G.; Breitenbach, J. M.; Lin, J.-S.; Cheng, Y.-C.; Kern, E. R.; Drach, J. C.; Zemlicka, J.
CORPORATE SOURCE: Dep. Chem., Wayne State Univ. Sch. Med., Detroit, MI, 48201-1379, USA
SOURCE: Antiviral Chemistry & Chemotherapy (1998), 9(4), 341-352
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: International Medical Press
DOCUMENT TYPE: Journal
LANGUAGE: English

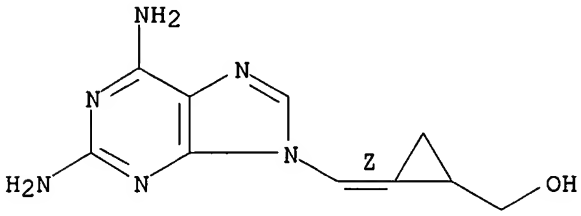
AB Several Z- and E-methylenecyclopropane nucleoside analogs were synthesized and tested for antiviral activity in vitro against human and murine cytomegalovirus (HCMV, MCMV), Epstein-Barr virus (EBV), varicella zoster virus (VZV), hepatitis B virus (HBV), herpes simplex virus types 1 and 2 (HSV-1, HSV-2), human herpesvirus 6 (HHV-6) and human immunodeficiency virus type 1 (HIV-1). The Z-2-amino-6-cyclopropylaminopurine analog was the most effective agent against HCMV (EC50 or EC90 0.4-2 .mu.M) followed by syncytol and the Z-2,6-diaminopurine analogs (EC50 or EC90 3.4-29 and 11-24 .mu.M) followed by syncytol and the Z-2,6-diaminopurine analogs (EC50 or EC90 3.4-29 and 11-24 .mu.M, resp.). The latter compd. was also a strong inhibitor of MCMV (EC50 0.6 .mu.M). Syncytol was the most potent against EBV (EC50 <0.41 and 2.5 .mu.M) followed by the Z-2,6-diaminopurine (EC50 1.5 and 6.9 .mu.M) and the Z-w-amino-6-cyclopropyl-aminopurine deriv. (EC50 11.8 .mu.M). Syncytol was also most effective against VZV (EC50 3.6 .mu.M). Activity against HSV-1, HSV-2 and HHV-6 was generally lower; synthymol had an EC50 of 2 .mu.M against HSV-1 (ELISA) and 1.3 .mu.M against EBV in Daudi cells but was inactive in other assays. The 2-amino-6-cyclopropylamino analog displayed EC50 values between 215 and >74 .mu.M in HSV-1 and HSV-2 assays. 2-Amino-6-cyclopropylaminopurine and 2,6-diaminopurine derivs. were effective against HBV (EC50 2 and 10 .mu.M, resp.), whereas none of the analogs inhibited HIV-1 at a higher virus load. Syncytol and the E isomer were equipotent against EBV in Daudi cells but the E isomer was much less effective in DNA hybridization assays. The E-2,6-diaminopurine analog and E isomer of synthymol were devoid of antiviral activity.

IT **210355-04-7P 210355-05-8P 213484-30-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of Z- and (E)(hydroxymethylcyclopropylidene)-methylpurines and pyrimidines as antiviral agents)

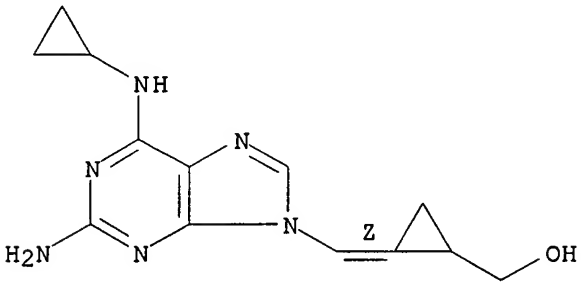
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.



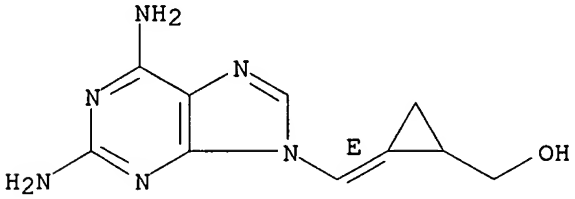
RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 213484-30-1 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

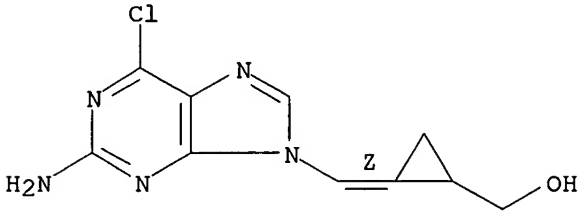


IT **200434-97-5 200435-01-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of Z- and (E)(hydroxymethylcyclopropylidene)-methylpurines and pyrimidines as antiviral agents)

RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-,

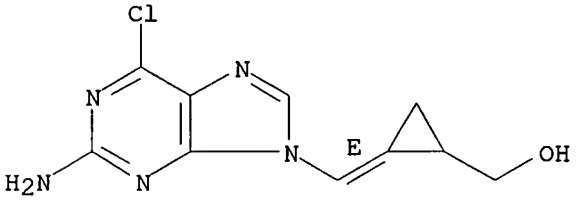
(2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



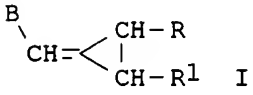
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:490642 HCAPLUS
DOCUMENT NUMBER: 129:122843
TITLE: Preparation of 2-hydroxymethylcyclopropylidenemethyl-purines and -pyrimidines as antiviral agents
INVENTOR(S): Zemlicka, Jiri; Qiu, Yao-ling; Drach, John C.; Ptak, Roger G.
PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA; Wayne State University; Zemlicka, Jiri; Qiu, Yao-Ling; Drach, John C.; Ptak, Roger G.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9830563	A1	19980716	WO 1998-US440	19980107
W: CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6352991	B1	20020305	US 1999-267839	19990312
US 2002193353	A1	20021219	US 2002-47202	20020114

PRIORITY APPLN. INFO.: US 1997-35826P P 19970108
US 1997-45676P P 19970506

WO 1998-US440 A2 19980107
US 1999-267839 A1 19990312
OTHER SOURCE(S): MARPAT 129:122843
GI

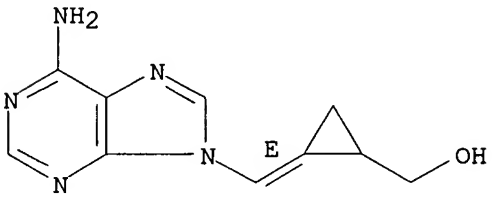


AB 2-Hydroxymethylcyclopropylidenemethyl nucleosides I (R = CH2OH, CH2OR2, R1 = H; R = H, R1 = CH2OH, CH2OR2; R2 = phosphates, B = purine or pyrimidine heterocyclic ring and is preferably selected from the group consisting of 6-aminopurine, 6-diaminopurine, 2-amino-6-cyclopropylaminopurine, 6-hydroxypurine (hypoxanthine), 2-amino-6-halo substituted purines, 2-amino-6-alkoxy substituted purines, 2-amino-6-hydroxypurine, 3-deazapurines, 7-deazapurines, 8-azapurines, cytosine, 5-halo substituted cytosines, 5-alkyl substituted cytosines, thymine, uracil and 6-azapyrimidines) were prepd. as virucides. Thus, syn-N9-(2-hydroxycyclopropylidenemethyl)guanine was prepd. and tested in vivo in mice as virucide against HIV-1 (IC50 = 0.8-1.3 .mu.M).

IT **200434-67-9P 200434-69-1P 200434-97-5P**
200435-01-4P 200496-39-5P 210355-01-4P
210355-04-7P 210355-05-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hydroxymethylcyclopropylidenemethylpurines and pyrimidines as antiviral agents)

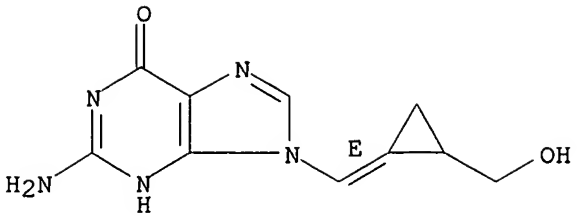
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



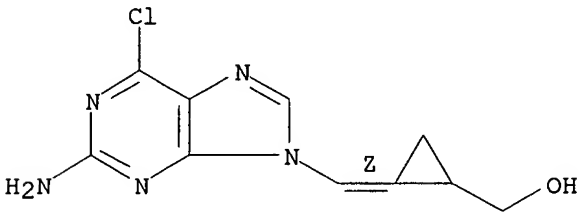
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



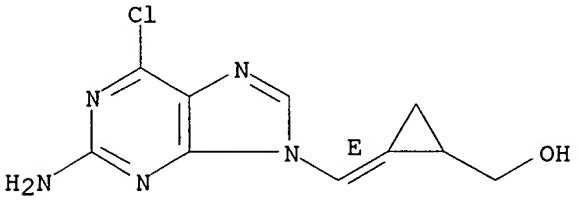
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



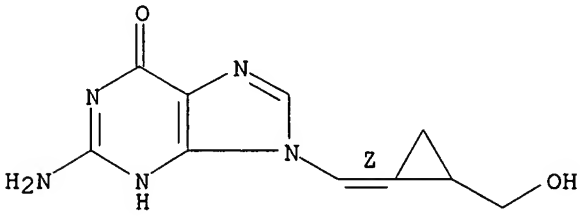
RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



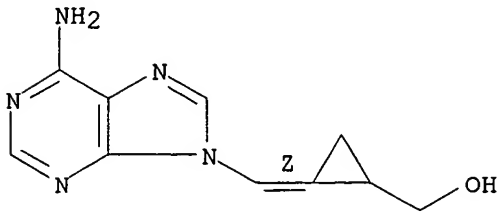
RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropyliden e]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.



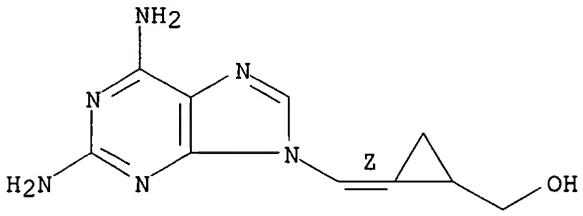
RN 210355-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



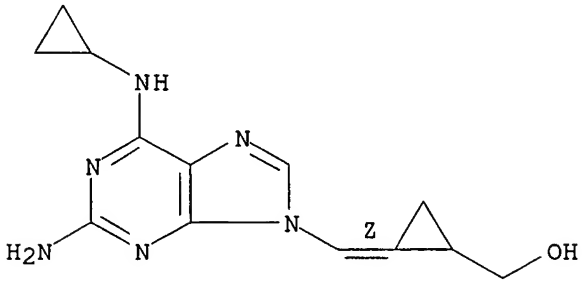
RN 210355-04-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(2,6-diamino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 210355-05-8 HCAPLUS
CN Cyclopropanemethanol, 2-[[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]methylene]-, (2Z)- (9CI) (CA INDEX NAME)

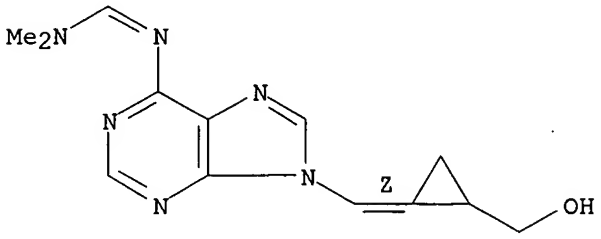
Double bond geometry as shown.



IT **200434-90-8P 200434-92-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hydroxymethylcyclopropylidenemethylpurines and pyrimidines as antiviral agents)
RN 200434-90-8 HCAPLUS
CN Methanimidamide, N'-[9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-

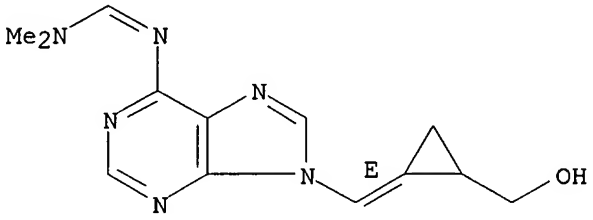
purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



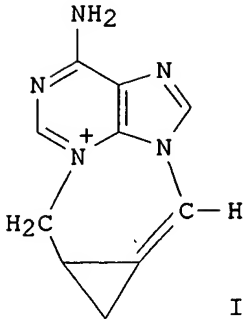
RN 200434-92-0 HCAPLUS
CN Methanimidamide, N'-[9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.

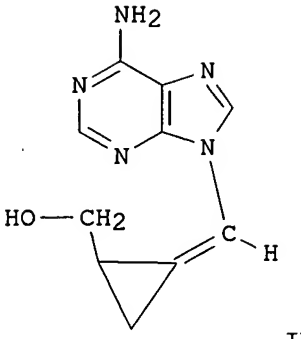


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:395196 HCAPLUS
DOCUMENT NUMBER: 129:161800
TITLE: 3,5'-Anhydrosynadenol: a polycyclic anhydronucleoside analog
AUTHOR(S): Qiu, Yao-Ling; Zemlicka, Jiri
CORPORATE SOURCE: Barbara Ann Karmanos Cancer Inst., Wayne State Univ. Sch. Med., Detroit, MI, 48301-1379, USA
SOURCE: Angewandte Chemie, International Edition (1998), 37(10), 1440-1441
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

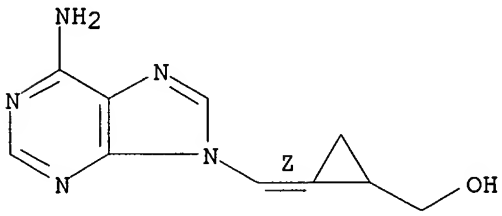
AB Formation of anhydronucleoside analog (I) from the syn-form of synadenol (II) is reported. Thus, II reacted smoothly with POCl3/PO(OMe)3 to give I, isolated as the acetate. Formation of I from II provides unambiguous proof that II has the Z configuration, important for the antiviral activity of II and its analogs, and also forms a novel polycyclic system contg. a methylenecyclopropane moiety.

IT **210355-01-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 3,5'-anhydrosynadenol as a polycyclic anhydronucleoside analog)

RN 210355-01-4 HCAPLUS

CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:122768 HCAPLUS

DOCUMENT NUMBER: 128:180622

TITLE: 9-Hydroxymethylcyclopropylidenemethylenyladenine: the design, facile synthesis, isomer separation and anti-HIV-1 activities

AUTHOR(S): Cheng, Changmei; Shimo, Tetsuro; Somekawa, Kenichi; Baba, Masanori

CORPORATE SOURCE: Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Kagoshima University, Kagoshmima, 890, Japan

SOURCE: Tetrahedron (1998), 54(10), 2031-2040
CODEN: TETRAB; ISSN: 0040-4020

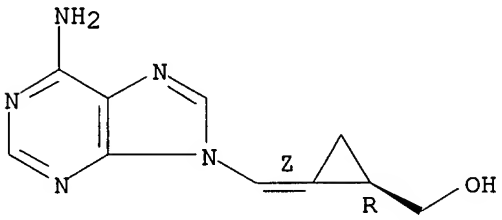
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 9-Hydroxymethylcyclopropylidenemethylenyladenine was designed based on the anal. of the structure-activity relationship and synthesized by coupling reaction of a vicinal dibromocyclopropane deriv. with adenine. The cis/trans isomers and an enantiomer of the cis-isomer of the cyclic .alpha., .beta.-unsatd. nucleosides derived by redn. were sepd. by reverse phase HPLC and chiral HPLC, resp. The cis-isomer was effective against HIV-1 and the (-)cis-isomer was highly effective with EC50 13 .mu.M.

IT **203305-34-4P 203305-37-7P 203305-38-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, facile synthesis, isomer sepn. and anti-HIV activity of 9-hydroxymethylcyclopropylidenemethylenyladenine)

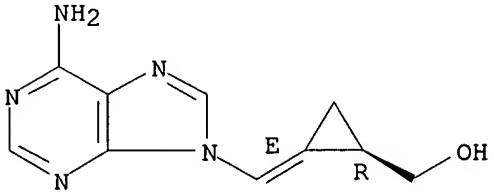
RN 203305-34-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



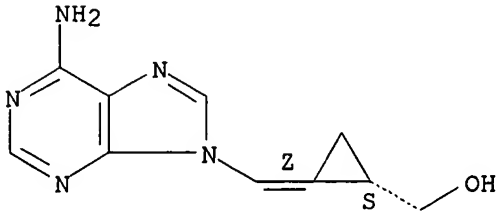
RN 203305-37-7 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1R,2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



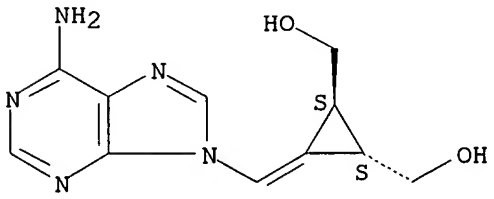
RN 203305-38-8 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (1S,2Z)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



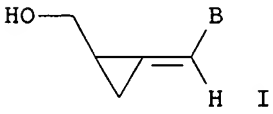
L16 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:24201 HCAPLUS
DOCUMENT NUMBER: 128:102328
TITLE: Reactions of methylenecyclopropanes with a diethylzinc-bromoform system, and the utilization for synthesis of a novel cyclopropylidene-nucleoside
AUTHOR(S): Cheng, Changmei; Shimo, Tetsuro; Somekawa, Kenichi; Kawaminami, Masaru
CORPORATE SOURCE: Kagoshima, 890, Japan
SOURCE: Tetrahedron Letters (1997), 38(52), 9005-9008
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reactions of substituted methylenecyclopropane with diethylzinc-bromoform gave bromospiro [2.2]pentane derivs., bromoform-addn. compds., an oxabicyclo-compd. and adjacent dibromo-compd., and the last product was derived to a novel .alpha., .beta.-unsatd. nucleoside.
IT **201273-54-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(reactions of methylenecyclopropanes with a diethylzinc-bromoform system and the utilization for synthesis of a novel cyclopropylidene-nucleoside)
RN 201273-54-3 HCAPLUS
CN 1,2-Cyclopropanedimethanol, 3-[(6-amino-9H-purin-9-yl)methylene]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L16 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:47 HCAPLUS
DOCUMENT NUMBER: 128:70379
TITLE: (Z)- and (E)-2-((Hydroxymethyl)cyclopropylidene)methyl adenine and -guanine. New Nucleoside Analogs with a Broad-Spectrum Antiviral Activity

AUTHOR(S): Qiu, Yao-Ling; Ksebati, Mohamad B.; Ptak, Roger G.; Fan, Boreas Y.; Breitenbach, Julie M.; Lin, Ju-Sheng; Cheng, Yung-Chi; Kern, Earl R.; Drach, John C.; Zemlicka, Jiri
CORPORATE SOURCE: Department of Chemistry Experimental and Clinical Chemotherapy Program, Barbara Ann Karmanos Cancer Institute Wayne State University School of Medicine, Detroit, MI, 48201-1379, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(1), 10-23
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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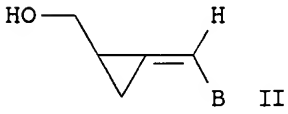
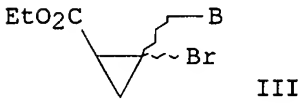
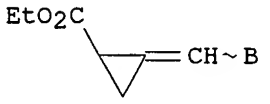


II



III



IV

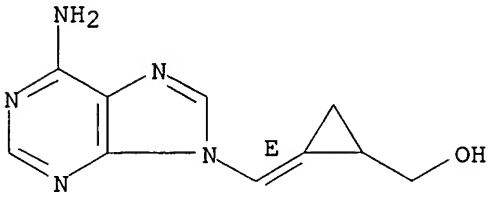
AB New nucleoside analogs I and II [B = adenin-9-yl (Ade), guanin-9-yl (Gua)] based on a methylenecyclopropane structure were synthesized and evaluated for antiviral activity. Reaction of 2,3-dibromopropene with adenine led to the corresponding bromoalkene, which was benzoylated to give the N6,N6-dibenzoyladenine deriv. Attempts to convert either adenine bromoalkene to the corresponding bromocyclopropane by reaction with Et diazoacetate catalyzed by Rh2(OAc)4 were futile. By contrast, cyclopropanation of 2,3-dibromopropene with Et diazoacetate afforded smoothly the dibromocyclopropanecarboxylic ester as a mixt. of E and Z isomers. Alkylation of the dibromocyclopropanecarboxylic esters with adenine gave (E)- and (Z)-bromo derivs. III (B = Ade). Base-catalyzed elimination of HBr resulted in the formation of (Z)- and (E)-methylenecyclopropanecarboxylic esters. More convenient one-pot alkylation-elimination of adenine or 2-amino-6-chloropurine with the above dibromocyclopropanecarboxylic esters afforded (Z)- and (E)-methylenecyclopropane derivs. IV. The Z-isomers were always predominant in these mixts. (Z/E .apprx. 2/1). Redn. of IV with DIBAL-H afforded (Z)- and (E)-methylenecyclopropane alcs. I and II. The latter were resolved directly by chromatog. The spectra of the Z-analogs I are consistent with an anti-like conformation of the nucleobases. By contrast, 1H NMR and IR spectra of bromo esters III (B = Ade) are indicative of syn-conformation of adenine. Several Z-(hydroxymethyl)methylenecyclopropanes exhibited in vitro antiviral activity in micromolar or submicromolar range against human and murine cytomegalovirus (HCMV and MCMV), Epstein-Barr virus (EBV), human herpes virus 6 (HHV-6), varicella zoster virus (VZV), and hepatitis B virus (HBV). Analogs I (B = Ade, Gua, 2-amino-6-chloropurin-9-yl) were the most

effective agents against HCMV (IC50 1-2.1, 0.04-2.1, and 0.8-5.6 .mu.M), MCMV (IC50 2.1, 0.3, and 0.3 .mu.M) and EBV in H-1 (IC50 0.2, 0.3, and 0.7 .mu.M) and Daudi cells (IC50 3.2, 5.6, and 1.2 .mu.M). Adenine analog I (B = Ade) was active against HBV (IC50 2 .mu.M), VZV (IC50 2.5), and HHV-6 (IC50 14 .mu.M). Synadenol (I; B = Ade) and the E-isomer II (B = Ade) were substrates of moderate efficiency for adenosine deaminase from calf intestine. The E-isomer II was more reactive than Z-isomer. The deamination of I (B = Ade) effectively stopped at 50% conversion. Synadenol was also deaminated by AMP deaminase from aspergillus sp.

IT **200434-67-9P 200434-69-1P 200496-39-5P,**
Synguanol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of stereoisomeric [(hydroxymethyl)cyclopropylidene]methyladenine and -guanine derivs. as new nucleoside analogs with broad-spectrum antiviral activity)

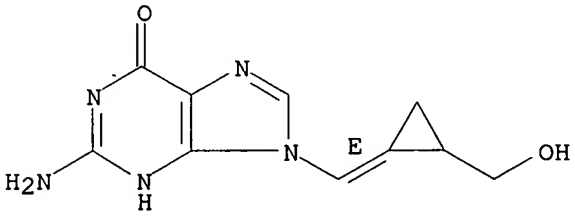
RN 200434-67-9 HCAPLUS
CN Cyclopropanemethanol, 2-[(6-amino-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



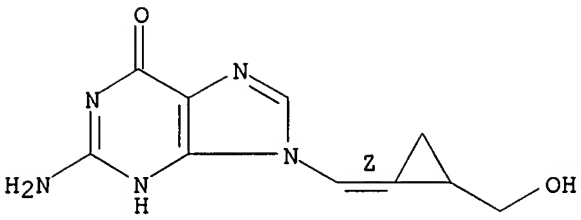
RN 200434-69-1 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 200496-39-5 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]- (9CI) (CA INDEX NAME)

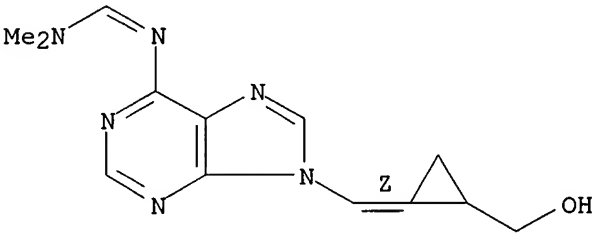
Double bond geometry as shown.
Currently available stereo shown.



IT **200434-90-8P 200434-92-0P 200434-97-5P**
200435-01-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of stereoisomeric [(hydroxymethyl)cyclopropylidene]methyladenine and -guanine derivs. as new nucleoside analogs with broad-spectrum antiviral activity)

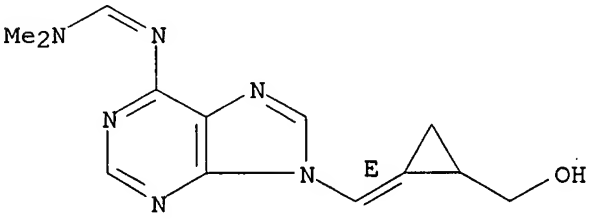
RN 200434-90-8 HCAPLUS
CN Methanimidamide, N'-[9-[(Z)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



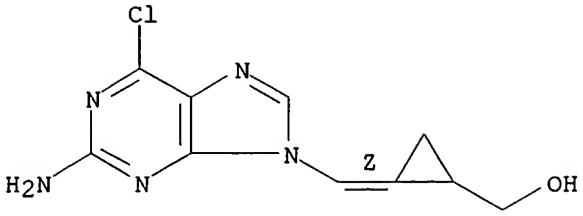
RN 200434-92-0 HCAPLUS
CN Methanimidamide, N'-[9-[(E)-[(hydroxymethyl)cyclopropylidene]methyl]-9H-purin-6-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Double bond geometry as described by E or Z.



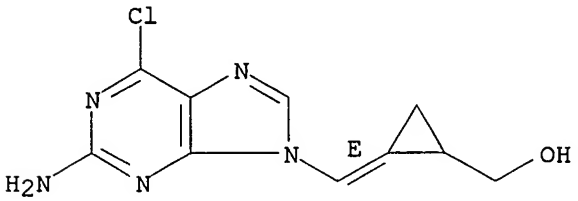
RN 200434-97-5 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 200435-01-4 HCAPLUS
CN Cyclopropanemethanol, 2-[(2-amino-6-chloro-9H-purin-9-yl)methylene]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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L13                 STR
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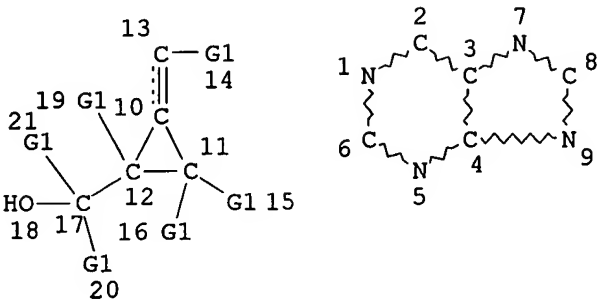


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L15           45 SEA FILE=REGISTRY SSS FUL L13
L16           20 SEA FILE=HCAPLUS ABB=ON  L15
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=> d his

     (FILE 'HOME' ENTERED AT 15:04:52 ON 10 JAN 2003)

     FILE 'HCAPLUS' ENTERED AT 15:05:08 ON 10 JAN 2003
                E ZEMLICKA JIRI/AU
L1           218 S E1,E3
                E QUI YAO/AU
                E QIU YAO/AU
L2            19 S E5
                E DRACH JOHN/AU
L3           180 S E3-5
                E PTAK ROGER/AU
L4            38 S E3-4
L5             6 S L1 AND L2 AND L3 AND L4
                SELECT RN L5 1-6
                SELECT RN L5 2

     FILE 'REGISTRY' ENTERED AT 15:08:15 ON 10 JAN 2003
L6            70 S E110-179

     FILE 'HCAPLUS' ENTERED AT 15:08:35 ON 10 JAN 2003
L7             6 S L5 AND L6

     FILE 'REGISTRY' ENTERED AT 15:16:30 ON 10 JAN 2003
L8                STR
L9             1 S L8
L10           45 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 15:26:08 ON 10 JAN 2003
L11           20 S L10

     FILE 'CAOLD' ENTERED AT 15:26:53 ON 10 JAN 2003
L12            0 S L11

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     FILE 'REGISTRY' ENTERED AT 15:38:36 ON 10 JAN 2003
L13               STR L8   see str. on dgue stat, attached
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     FILE 'HCAPLUS' ENTERED AT 15:43:12 ON 10 JAN 2003
L16           20 S L15  20 cits, attached
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